1928

ARCHIVES OF DISEASE IN CHILDHOOD.

Vol. 3. AUGUST, 1928. No. 16.

CONTENTS

ISSUED BY THE BRITISH MEDICAL ASSOCIATION.

London: British Medical Association House, Tavistock Square, W.C. 1.

Yearly Subscription (6 numbers), 25/- *Single Number, 5/-*

NOTICE TO SUBSCRIBERS.

Subscriptions are payable to the Financial Manager of the British Medical Association who has charge of all financial matters concerning the ARCHIVES OF DISEASE IN CHILDHOOD. Address: British Medical Association House, Tavistock Square, London, W.C. 1.

NOTICE TO CONTRIBUTORS.

All papers submitted for publication should be sent to Dr. Reginald Miller, 110, Harley Street, W. 1. All other editorial matters should be referred to Dr. Hugh Thursfield, 84, Wimpole Street, W. 1.

Papers sent for publication should be typewritten. Illustrations will usually be inserted in the text itself, and care should be taken that the text is marked to show the desired position of each illustration.

Charts and curves accompanying papers should be carefully drawn, on white paper. Any lettering on these drawings should be lightly inserted in pencil.

Contributors will receive one proof in page, but it is assumed that all but verbal corrections have been made in the original manuscript; an allowance at the rate of ten shillings per sheet of sixteen pages is made for alterations in the proof (printer's errors excepted), and contributors will be responsible for any excess.

Contributors will be supplied with reprints of their articles at cost price if application is made when returning proofs. An estimate of costs will be given if desired on application to the Financial Manager of the British Medical Association.

Papers which have been published become the property of the ARCHIVES and permission to republish must be obtained from the Editors.

THE LÆVULOSE TOLERANCE OF CONVALESCENT CHILDREN: WITH SPECIAL REFERENCE TO RHEUMATISM.

BY

R. TAYLOR CHADWICK, M.A., B.CHIR.

The investigations described in this paper were undertaken with the object of providing some answer to the question, 'Is there, in the child of rheumatic diathesis, some constitutional abnormality of hepatic function?'

A considerable amount of literature has been produced in connection with the testing of the function of the liver, and several methods have been devised, but almost all the work has been carried out on adults suffering from severe anatomical and pathological changes in the organ. References to disease in children are few, and confined to severe instances.

Of the tests of hepatic function that of the tolerance to lævulose appears to stand on the firmest footing, and in modified forms has now been in use for many years. In 1901, Strauss[1] considered that the administration of lævulose and its detection in the urine was a test of liver function. But the renal threshold for lævulose is low, and many normal persons pass it in the urine after oral administration. Later observers have employed the more accurate method of estimating the blood sugar after oral ingestion of lævulose: Schirokauer[2], MacLean and de Wesselow[3], Spence and Brett[4], Tallerman[5], King[6] and others. Rolleston[7] has stated that lævulose is the only sugar which cannot be dealt with elsewhere in the body than in the liver. MacLean and de Wesselow have stated that lævulose is the only sugar which does not cause a rise in blood sugar when taken by healthy persons.

Certain observers have little faith in the test, but there is much concrete evidence that such views are untenable.

PRESENT INVESTIGATIONS.

Nature of Material Investigated. Group I. In order to obtain figures for the effects of lævulose on non-rheumatic children, a number of tests have been made on convalescent or recovered cases of infantile paralysis, tuberculous peritonitis, tuberculous arthritis, bronchiectasis. The paralysis cases were of very long standing, and, except for their deformities could be regarded as healthy children. Certain of the other cases were of an active type, others could be considered quiescent.

Group II. For the rheumatic groups, children of several types have been employed. Classification as follows has been adopted as far as possible:—

(i) Rheumatism without residual heart lesion.
(ii) Rheumatism with residual heart lesion.
(iii) Chorea without residual heart lesion.
(iv) Chorea with residual heart lesion.

Practically all the rheumatic children tested have been of the recovering type, though in a few instances it has been possible to test cases clinically active. In several instances there was definite clinical evidence of relapse, and opportunity was taken of testing during these periods.

Throughout the investigations note has been taken of the clinical condition of the cases at the times of testing and during the intervening periods.

Many of the children have remained under supervision for long periods, some as long as six months, so that it has been possible to perform tests on more than one occasion in the same subject. This fact has elucidated findings which at first sight were confusing.

The Dosage and Administration of Lævulose. By preliminary trials it was found that doses of 20 to 30 grm. of lævulose dissolved in 100 c.cm. of water were sufficient to cause a satisfactory rise in the value of the blood sugar. A drachm of fresh lemon juice was added to the fluid, and the resulting 'lemonade' was readily taken by the children. Standard doses of 20, 25, or 30 grm. were given according to the size of the child. Larger doses than 30 grm. were tried for the larger children over 13 years of age, but the results were no better than with the smaller standard dose.

The Method of Estimating the Blood Sugar. For blood-sugar estimation, the Hagedorn-Jensen method has been used. The technique is easy of performance, and the quantity of blood used, 0.1 c.c., is readily obtained from small children. (A full account of the method and reagents is given in Cole's Practical Biochemistry, Cambridge University Press.)

Arrangements for the Test Subjects. A considerable amount of preparation has been found necessary in order to obtain satisfactory resting values for blood sugar in many of the children. Conditions of equanimity in mind and body are essential if concordant results are to be obtained. The following routine has been adapted :—

(1) Rest in bed for at least six hours before commencement of test. In bed during test.
(2) Abstention from food of any kind for at least five hours before testing and during testing.
(3) Enough water for drinking to quench thirst.
(4) Books provided for reading, or small toys, etc., to keep child amused.
(5) Two or more children undergoing test at the same time. In a small side ward for preference.

Details of Blood Samples. As a routine four to six samples of blood have been taken, one before the drinking of the lævulose solution, to give resting blood-sugar value, and the remainder at half-hourly intervals. Blood has been taken by stabbing the skin of the thumb, just above the nail on the dorsal surface, after engorgement by shaking and wrapping a piece of rubber tubing round the base of the thumb. A straight triangular skin needle, carried in the cork of a bottle containing ether for cleaning up the skin, has been found satisfactory. The drops of blood were received into a small porcelain crucible containing a trace of potassium oxalate ground fine to prevent clotting.

Results of Investigations.

Brief clinical notes of the thirty-five cases tested are given, the cases being classified into the groups already described. The blood-sugar readings are given in the tables (Tables I—V). In these the dates of the tests have not been given, but where repeated tests were made, the intervals between them have been indicated. The various tests have been carried out in the last two years, as the supply of material availed.

Group I. Non-Rheumatic Children (see Table I.)

Case 1. Harold C. 10. Infantile Paralysis of old standing. Paralysis left arm. Otherwise healthy.

Case 2. Robert W. 10. Infantile paralysis of old standing. Paralysis of both legs. In good health otherwise.

Case 3. Blanche W. 14. Infantile paralysis of old standing. Paralysis of both legs. A nervous child. In good health.

Case 4. Celia O. 13. Tuberculous right knee joint, recently active. On extension splint. Joint apparently now quiescent.

Case 5. Andrew L. 10. Bronchiectasis. Active. Much foul, purulent sputum, very marked clubbing of the toes and fingers.

Case 6. George A. 12. Bronchiectasis. Quiescent. Boy up and about, slight cough in the mornings, with a little sputum. Medium clubbing of the fingers and toes.

Case 7. John B. 10. Healed tuberculous peritonitis. Onset of disease one year ago. No signs of activity at present. No digestive disturbance, is putting on weight and looks well.

Case 8. Eddie P. 9. Recent tuberculous peritonitis. 9 months' history, moderately severe. Boy looks unwell, very pale. No diarrhœa, good appetite, weight increasing. Abdomen a little resistant and doughy.

One month later, improved. Abdomen quite soft.

Case 9. Eric T. 12. Healed tubercle of the carpus and flexor tendons of the right side.

Group II. Rheumatic Cases (see Tables II—V.)

(*i*) *Convalescent Acute Rheumatism without detectable heart lesion at time of testing.* (See Table II).

Case 10. Veronica L. 11. Two months ago had acute rheumatic pains and swellings of knees. Kept in bed at home. At time of examination, no pains, no joint swelling, heart not enlarged, no heart murmurs, liver not enlarged. Child pale.

Case 11. Eva B. 12. Six weeks ago, acute rheumatic pains, and joint swellings. Kept in bed at home. First attack. At time of examination, no pain, no joint swelling, heart not enlarged, no murmurs, liver not enlarged. Throat and tonsils inflamed.

(*ii*) *Convalescent Rheumatic Children, with Cardiac Abnormalities at the time of testing.* (See Table III.)

Case 12. Florence S. 12. Rheumatism with transient Heart affection. Nine months ago had attack of sore throat, followed by swelling of the ankles, and growing pains. Was kept in bed 14 weeks. Heart diagnosed at hospital as being affected. On examination :—Dark, well looking, well covered girl. Teeth and tonsils healthy. Heart slightly enlarged, impulse not forcible, localised. Soft mitral systolic murmur conducted half across axilla. Pulmonary second sound not accentuated, aortic sound natural. No growing pains, no joint affections.

One month later. Feels well. Rapidly putting on weight. Commencing light physical exercises. The heart sounds are now natural, there is no mitral systolic murmur, and the enlargement has gone.

Three months later. Temperature irregular, after being subnormal since admission. Throat reddened, but not sore, no pains, no joint swellings. Heart impulse forcible, pulse rate increased. Return of mitral systolic murmur.

Two months later. Temperature now regular and subnormal. Cardiac impulse slight and localised. No murmur.

CASE 13. Annie H. 12. Rheumatism with persistent endocarditis. Two years ago first attack of rheumatic fever, which was slight. Three months ago, second attack, lasting six weeks. Pain and swelling in hands, elbows, feet and knees. Returned to school for short time before admission. On examination :—Tall, fair, pale child. Teeth good, tonsils ragged and slightly enlarged. Heart, pulse rapid, cardiac impulse forcible, diffuse, no thrills palpable. Heart enlarged, sounds loud, short mitral systolic murmur, presystolic murmur, long rough pulmonary systolic murmur. Aortic sounds natural. Liver not enlarged.

One month later. Clinically improving. A definite mitral presystolic murmur was heard at time of testing, and confirmed at later dates. Temperature irregular.

Three weeks later. Forcible and sustained cardiac impulse. Established double mitral murmur. No pains or joint swellings. Throat less inflamed. Child's term of stay terminated.

CASE 14. Bertha R. 13. Sub-acute rheumatism with endocarditis. First attack of rheumatism at the age of six. Since then has suffered from repeated attacks of growing pains, and joint swellings. Never choreic. On examination :—Tall, pale girl, lips and ears bluish. No respiratory distress. No joint pains at present, but had some a week ago. Tonsils much enlarged. Heart : short, sharp cardiac impulse, localized, slight presystolic thrill. Heart not enlarged. Mitral first sound short, loud, mitral systolic and presystolic murmurs, pulmonary second sound accentuated no murmur, aortic second natural. Liver not enlarged.

Three weeks later. Child much improved. Temperature regular and subnormal pulse slowed down. Cyanosis has disappeared. No pain.

Two glucose tolerance tests were carried out on this case one week after each of the lævulose tests respectively. They showed no departure from the type of curve given by a healthy person.

CASE 15. Annie G. 9½. Endocarditis following measles. 14 months ago, attack of measles. 1 month ago, marked roughening of the first sound in the mitral area. No signs to explain same. No enlargement of the heart. Just before testing, a definite diagnosis of mitral stenosis, with enlargement of the right side of the heart was made. There were no growing pains or other rheumatic phenomena. No enlargement of the liver.

One fortnight later. No apparent change in the clinical condition. After 2½ hours blood sugar reached ·092%.

Three months later. There has been a definite improvement in the general condition of the child. Gain in weight, no rheumatic manifestations. Heart condition one of established mitral stenosis.

CASE 16. George D. 9. Acute rheumatism with transient heart murmur. Six months ago, first attack of rheumatism. Both ankles swollen and painful. Heart developed transient mitral systolic murmur. Boy had prolonged continuous hospital bed treatment till admission to convalescent home. No signs of active rheumatism recently. On examination. A pale boy, though not anæmic. No growing pains or swollen joints. Heart not enlarged, no murmurs. Liver not enlarged. Throat healthy, tonsils recently removed.

Three weeks later. Boy active, and getting up all day. Looks considerably better. No signs of active rheumatism. Heart, no murmurs, pulse rate steady and not rapid.

CASE 17. Alfred W. 12. Severe rheumatism with cardiac lesions. Rheumatism commenced six months ago. Sore throat, pain and swelling of joints. Treated by private doctor who stated that at the time there was no severe heart lesion. When seen at the Out-patients rheumatic clinic, was very pale, with inflamed throat, enlarged tonsils. Back of right hand puffy, no swollen joints. Heart dilated, sounds hurried and loud, double mitral valve lesion, a loud pulmonary systolic murmur, nil abnormal in the aortic sound. He was kept under treatment for just over a month in bed. When examined before testing, the heart was less dilated, double murmurs could be heard over the mitral and aortic regions. The temperature had settled down, but the pulse remained rapid. No pains recently.

One month later. Considerable improvement in the clinical condition. The boy has put on weight, the pulse rate is lower, temperature regular. No pain.

The boy continued to attend Out-patients for a few months after discharge from hospital, and did well, but nine months after these tests were carried out, there was a severe relapse, and the boy died.

Case 18. Dorothy E. 8. Severe cardiac rheumatism with relapse. A severely ill child, with joint swellings and pains, nodules on the hands and knees, rapid pulse, raised temperature. Heart dilated, pericardial friction, severe lesions of the mitral and aortic valves. Compression of the left base of the lungs, with many moist bronchial sounds. Liver slightly enlarged, palpable ½ inch below the costal margin. The child had suffered from recurrent rheumatism for the last two years, and had spent most of her time in bed.

Four blood sugar values were obtained, when it was decided to discontinue testing, as the child's condition was bad.

Case 19. Norah S. 12. Recurrent rheumatism with cardiac lesion. Child has suffered from recurrent attacks of growing pains and swollen joints for the last two years. On examination. A tall, thin child. No pains, no joint swellings. Tonsils large and ragged Heart slightly enlarged, a loud conducted mitral systolic murmur, pulmonary second sound accentuated. Nil abnormal at the aortic area. Pulse rate normal.

Case 20. Stella B. 11. Rheumatic endocarditis. Three months ago, started to have pain in the left side and head, with loss of weight and energy. No joint swellings, but transient pains in the limbs. When first seen at this time, the heart was dilated and there was a loud, rough mitral systolic murmur. On examination :—three months after first seen. Dark, well made girl. No pain or joint lesions. Heart enlarged, with mitral systolic and diastolic murmurs, and loud pulmonary systolic murmur.

Two months later. Great clinical improvement. No signs of active disease. Heart much smaller. Still double mitral murmur. Temperature now steady.

This girl has been watched in Out-patients for the last year. There has been no relapse, and the general condition has been excellent. The heart murmurs have disappeared.

Case 21. Sarah C. 11. Acute rheumatic endocarditis. Rheumatic history vague. Nervous, getting thinner, paler. On examination :—An anæmic, nervous child. Tonsils enlarged and inflamed. No joint lesions, or pains. Heart not enlarged, no thrills. Mitral systolic and presystolic murmurs, with accentuated pulmonary second sound. Not a congenital heart.

One month later. Child has had an attack of acute tonsillitis. No pains or joint lesions, but the heart dilated and developed a double mitral murmur. Lævulose testing was carried out one month after the previous test, and one week after the sore throat had developed.

Three months later. Tonsillectomy one month previous to test. At the time of the test, the heart was not dilated, there was an established double mitral lesion. The electrocardiogram was normal, and the child's clinical condition much improved.

Case 22. Kathleen K. 11. Rheumatic endocarditis. History scanty. Child had had acute rheumatism about two years ago, was treated at home. On examination :—Well covered girl, no cyanosis, tonsils large, teeth carious. Heart not enlarged, no thrill, a loud mitral systolic murmur, conducted to posterior border of the left axilla.

One month later. Child improving.

Case 23. Jack M. 11. Rheumatic endocarditis. About one year's history of growing pains, swelling of the ankles and knees. Treated at home. On examination :—A pale, thin boy, looks ill. No pains or joint swellings, tonsils large and ragged, cervical glands enlarged. Heart, dilated, rapid, with double mitral murmur. Temperature and pulse irregular.

Three weeks later. Clinical condition improving. Heart not so dilated. Temperature and pulse settling.

Case 24. John H. 9. Chronic rheumatism with endocarditis. History of growing pains over the last three years. Has been absent from school on many occasions. Easily tired and gets badly out of breath on exertion. On examination :—A well-built boy, who has lost weight. Face and ears cyanosed. Tonsils large and inflamed. Heart not enlarged, sharp impulse, localized. Double mitral murmur, presystolic element well marked. At present is having pains in the legs, with slight swelling of the ankles.

One month later. Still has occasional growing pains in the legs, especially when the weather is damp. The boy is being kept in bed. At 2 hr. 20 min., blood sugar reached ·102%.

Boy's term of stay finished and there was no opportunity of retesting at a later date.

Case 25. Robert J. 9. Chronic rheumatism with endocarditis. Two years history of cardiac rheumatism. Has been almost continuously under hospital treatment. On examination :—Very dark, cyanotic boy. No pain at present, but short of breath on exertion. Heart

enlarged, with loud blowing mitral systolic murmur, conducted into the axilla. Second sound reduplicated.

One month later. The heart is less dilated, the mitral systolic murmur is louder, and the pulmonary second sound is much accentuated.

Three weeks later. The boy had pain and swelling in the right wrist for a week previous to this test. The heart dilated again, and a presystolic murmur appeared. The pulse and temperature were irregular. After 2½ hrs. the blood sugar was ·093.

One month later. No further signs of active rheumatism. The presystolic murmur has persisted.

(*iii*) *Cases of Chorea without Heart Lesion* (See Table IV).

This is again a small group, and the cases show rather unexpected results. Their behaviour is more like that of the non-rheumatic children, as opposed to the intolerance of the rheumatic and choreic cardiac groups.

Case 26. Elsie B. 7½. Recent chorea. Eleven weeks ago commenced with chorea of moderate intensity, affecting the limbs and face. Previously had been quite healthy. On examination :—Small girl, well covered. Slight choreiform movements of the tongue and face still present. No clinical heart lesion.

Case 27. Clarice A. 9. Recent chorea. 12 weeks ago began to have twitchings of left hand, leg and the face. Was able to feed herself. No history of growing pains. On examination :—A moderate degree of chorea in face, left arm and leg. Pulse and temperature regular. No clinical heart lesion.

Case 28. Eva C. 12. Persistent chorea. The child has suffered from chorea almost persistently for the last twelve months. Movements of the hands and face, to a lesser degree of the legs. There have been occasional growing pains in the legs and feet at various times, but no swelling of the joints. On examination :—A tall, rather thin girl. Movements of hands and face. No pain. Heart not clinically implicated.

Case 29. Ada K. 13. Persistent chorea. Persistent, jerky movements of all limbs, face and tongue for the last six months. Very resistant to treatment. No growing pains at any time. On examination :—A tall, well-built girl. Generalized choreiform movements of all the limbs of severe degree. Can only feed herself with difficulty. No clinical heart lesion.

(*iv*) *Cases of Chorea with residual Heart Lesion* (see Table V.)

This is a much more extensive group than the foregoing. It has been possible to keep the cases under observation for longer periods. The intolerance to lævulose is found to agree closely with that of the frank rheumatic group.

Case 30. Ruby W. 12. Chorea with transient heart lesion. Nine months' history. Recurrent sore throats, with pain and swelling of right knee. In bed for a few days at first, and was kept away from school. Developed choreiform movements a few weeks before admission to institution. On examination :—A well looking, well covered girl. Slight, generalized choreiform movements. Tonsils enlarged and ragged. Heart not enlarged, sounds high-pitched, with a short, soft mitral systolic murmur. Liver not enlarged.

Two months later. The girl has improved greatly. There are no choreiform movements now, and the systolic murmur has disappeared.

Five months later. The condition of the girl continues good. No return of the chorea. No change in the heart. On light physical exercises.

Case 31. Edith J. 13. Chorea following scarlet fever. 2½ years ago, scarlet fever. 2 years ago, first attack of chorea, lasting two months. 3 months ago, second attack of chorea of severe intensity. On examination :—Pale, tall, thin girl. Slight choreiform movements of face and upper limbs. Tonsils large and ragged. Heart, impulse forcible and diffuse, sounds loud and booming, with a mitral systolic murmur, and accentuated pulmonary second sound. Liver not enlarged.

A fortnight later. Girl has improved considerably with continuous bed treatment. Very little chorea now. No murmur in the heart, which is much less forcible.

Case 32. Nellie H. Recurrent chorea and mitral disease. Onset of moderately severe chorea one year ago, which has recurred at times since. On examination :—Very slight choreiform movements noticed. Heart not enlarged, but there is a loud mitral systolic murmur, conducted to the axilla.

Case 33. Elizabeth J. 12. Chorea with rheumatic pains. Two months ago, onset of severe jerky movements of the arms and legs. Pains in the arms and thighs. Heart not enlarged, pulse rapid, soft mitral systolic murmur. Alimentary tract healthy. Tonsils enlarged.

This girl has been watched for a year in the Out-patient department, and has had relapses of the chorea, with attacks of growing pains. The heart condition appears to be one of developing mitral stenosis.

Case 34. Alfred J. 10. Acute chorea, with rheumatism. Attack of rheumatism with moderate degree of chorea commenced about one month ago. Growing pains in the legs and ankles, with swelling of the latter. Jerky movements of the hands and face. Heart, tone poor with a faint mitral systolic murmur, and accentuated pulmonary second sound.

One month later. Quite steady, no movements of the arms or face. No pains in the lower limbs. The heart murmur has disappeared, the tone has improved.

Case 35. Arthur R. 11. Chorea and mitral disease. History of onset not obtained. At time of examination: Moderate degree of chorea of the limbs. Heart slightly enlarged, fair tone. Mitral systolic murmur conducted to the axilla.

One month later. Chorea much less marked. Heart condition unchanged.

Discussion.

Lævulose tolerance tests have been performed on 35 children, 9 cases being controls, 4 cases of simple chorea, 22 of rheumatism or chorea with signs of heart involvement. In addition to the children described in this paper similar tests have been performed on some 30 other children suffering from rheumatism, whose blood-sugar curves show the same results and have been omitted for sake of brevity.

Group I. Considering first the non-rheumatic control children, cases of old-standing infantile paralysis were chosen as controls since they showed no signs of disease except their residual deformities. In two of the cases there was no rise in the blood sugar; in one, a child of unstable blood sugar, there was a rise of 0·019 grm. per cent.

One case of tuberculosis of the knee, apparently quiescent, showed a rise of 0·005 grm. per cent. One case of quiescent abdominal tuberculosis showed a rise of 0·003 grm. per cent. A similar case, but showing signs of active disease, showed a rise of 0·022 grm. per cent.; one month later when the condition had much improved there was a rise of only 0·001 grm. per cent. One case of tuberculosis of the wrist, healed at time of examination showed a rise of 0·036 grm.

One case of active bronchiectasis showed a rise of only 0·005 grm., and a quiescent case showed no rise, but a drop, in the value.

In testing the cases with bronchiectasis and tuberculosis it was thought that a long continued infective process might have shown itself in some failure of liver function, but the only case to show any such evidence was one in which the tuberculous process could be taken as active.

It was also thought probable in the bronchiectasis cases that the venous stasis which was very marked in the hands and toes might be demonstrable in the liver, but there are no evidences of ill-effects on sugar function.

Group II. Considering secondly the cases of chorea and rheumatism, there is a sharp line of demarcation into two groups, those of simple chorea, and those of rheumatism with or without heart involvement and of chorea with heart involvement.

Simple chorea. Two of the cases with a recent history and active at the time of examination showed only 0·004 and 0·003 grm. per cent. rise in sugar value. Two very persistent cases showed rises of 0·009 and 0·021 grm. respectively. The latter case has been watched in out-patients for nearly two years and still suffers from twitching of a marked degree.

Rheumatism with and without heart involvement and chorea with heart involvement. This group, which comprises the largest in the series, differs from the earlier classification into four groups, owing to the similar results found in rheumatism, simple and complicated, and chorea with heart disease. In many of the children tested there was found a definite intolerance to lævulose. Certain of the cases have been followed for several months, and there was found a diminishing of the intolerance as clinical improvement took place. The intolerance did not follow the severity of the heart affection in respect of the valvular lesion, but seemed to bear a relationship to the dilatation and state of tone of the muscle. Thus a heart which was toxic and recovering from a recent bout of disease was associated with a much more marked intolerance to lævulose, and the same statement applied to a child recovering from recent rheumatism without clinical evidence of heart affection. Similarly, a child recovering from chorea with a residual heart lesion showed a more marked intolerance than one who could be regarded as quiescent.

There were in the cases tested no instances of jaundice, and in two cases only was there clinical evidence of enlargement of the liver, namely, Cases 18 and 25, both children showing intolerance. Three cases were examined during a relapse of rheumatism, namely, Cases 12, 24 and 25, and curves showing a return to a state of improved tolerance obtained. Case 18 was examined during a very severe relapse, and died three weeks after the test.

Two cases of rheumatism without detectable cardiac lesion were tested. In both there was a considerable rise in the sugar value, 0·036 and 0·085 grm. per cent.; here the rheumatic attack had been recent.

Turning to the cases of rheumatism with cardiac lesion, it is found that there is considerable variation in the rise of the blood sugar. In the more recent cases a rise of as much as 0·096 grm. per cent. (Case 19) was recorded though figures below 0·06 grm. per cent. were more usual. In cases watched over a period of several months it was found that there is a progressive fall in the intolerance, e.g., Case 12, who showed an increased intolerance during a slight relapse and a return to a flat curve later (Cases 15 and 20), as the clinical condition improved.

When there was clinical evidence of quiescence of the rheumatic process the children showed very little or no rise in blood sugar value after a dose of lævulose which previously caused an appreciable rise in that value, e.g., Cases 12, 16, 20 and 21. It will also be noted that the curve tended to be higher in those cases who had previously shown a number of relapses.

Cases of chorea with heart signs were closely comparable with those of rheumatism with similar heart condition, though the rise in the blood sugar was generally not so marked, rarely exceeding 0·03 grm. per cent. The same tendency to a return of a flat type curve was shown.

The time of the maximum value of the blood sugar was shown to vary in the different cases and in the same case. The most common time for the maximum to occur was at the end of the first hour, but a proportion of the cases were later, at the hour and a half. In some of the more severe cases there was a prolongation of the curve beyond two hours before return to the normal value. A possible explanation of this delay may perhaps lie in an inability of the intestine to absorb lævulose at the usual rate, or perhaps to a state of increasing saturation of a liver unable to deal with lævulose in quantity.

Very different figures have been given for rise of blood-sugar values which may be taken as showing hepatic intolerance to lævulose. Certain observers state that there should be no rise in value in the normal person, Maclean and de Wesselow[3]. Tallerman[5] gives a value of 30 mgrm. in his paper. Brown[8] in her recent paper gives a value of 30 mgrm. It is interesting to note that she quotes three cases of acute convalescent rheumatism in this paper with rises of 0·012, 0·022, and 0·027 grm. per cent. None of these cases had a heart lesion. Taking into consideration the figures for normal children and quiescent rheumatism given for the cases described in this paper, a value of 20 mgrm. rise more than covers the range.

In fact, with the exception of the cases of simple chorea given above, there would appear to be no intolerance to lævulose in those children who could be classed as well. When, however, the rheumatic process is active from a clinical standpoint, or when the child is recovering from a phase of rheumatic activity, there is intolerance to a greater or lesser degree.

Why the tolerance to lævulose should be upset in the rheumatic child, and should return to normal when the disease process is quiescent, are questions difficult to answer. The effects do not appear to be due to alimentary disturbance, as all the children were on a good diet, and there was no evidence of alimentary derangement. The question of tonsillar sepsis and enlargement appears to have some bearing on the subject, as most of the cases have had large and inflamed tonsils, though intolerance has been found in some cases whose tonsils have been removed. The suggestion is put forward for what it is worth, that the lævulose intolerance is due to toxic absorption from the tonsils, the heart, or other nidus of rheumatic infection.

Summary.

1. Details are given of lævulose tolerance tests carried out on healthy control children, and on cases of active disease, especially rheumatism.

2. Figures are given to show that in the healthy child, the child suffering from simple chorea and the child who has recovered from rheumatism, administration of lævulose has little or no effect on the blood sugar.

3. In the child with active rheumatism, with or without heart affection, and in the child with chorea and heart affection, there is an appreciable intolerance to lævulose.

4. The suggestion is made that intolerance to lævulose is due to toxic absorption from some focus of rheumatic infection.

The thanks of the writer are due to Dr. A. Dingwall Fordyce for his interest in this work, to the Committees of the Childrens' Convalescent Home, West Kirby, and of the Royal Liverpool Childrens' Hospital, Heswall, for their grants of apparatus and materials, and to the Merseyside Committee for Rheumatism for a financial grant.

REFERENCES.

1. Strauss, H., *Deutsch. Med. Wchnschr.*, Leipsic, 1901, XXVII, 757.
2. Schirokauer, H., *Ztschr. f. klin. Med.*, Berlin, 1913, LXXVIII, 462.
3. Maclean, H., & de Wesselow, O. L. V., *Quart. J. Med.*, Oxf., 1920, XIV, 103.
4. Spence, J. C., & Brett, P. C., *Lancet*, Lond., 1921, ii, 1362.
5. Tallerman, K. H., *Quart. J. Med.*, Oxf., 1923, XVII, 37.
6. King, *Lancet*, Lond., 1927, i, 385.
7. Rolleston, H. D., *St. Bart. Hosp. Rep.*, Lond., 1923, XXXVI, 35.
8. Brown, M. J., *Arch. Dis. Child.*, Lond., 1928, III, 81.

TABLE I. LÆVULOSE TEST: CONVALESCENT NON-RHEUMATIC CHILDREN.

Case No.	Clinical Notes.	Lævulose. Grm.	Percentage of Sugar in the Blood. Fasting.	Hours after lævulose. ½	1	1½	2
1	Inf. Paralysis (old)	25	·106	·079	·088	·088	·088
2	,, ,, ,, ...	25	·088	·079	·077	·088	·079
3	,, ,, ,, ...	30	·135	·121	·135	·119	·116
4	Tub. arthritis (quiescent)	30	·095	·099	·100	·093	·083
5	Bronchiectasis	25	·097	·102	·093	·097	·093
6	,, ...	30	·099	·092	·097	·099	·097
7	Tub. peritonitis (healed)	25	·113	·116	·107	·104	·099
8	,, ,, (recent)	25	·095	·106	·104	·127	·095
	,, ,, 1 month later (improved)	25	·106	·106	·107	·102	·097
9	Tub. arthritis (healed)		·127	·141	·145	·109	·109

TABLE II. LÆVULOSE TEST: CONVALESCENT RHEUMATIC CHILDREN, WITHOUT HEART LESION.

Case No.	Clinical Notes.	Lævulose. Grm.	Percentage of Sugar in the Blood. Fasting.	Hours after lævulose. ½	1	1½	2
10	Ac. rheumatism (convalescent) ..	25	·115	·146	·146	·141	·123
11	,, ,, ,, ...	25	·115	·200	·196	·164	·127

TABLE III. LÆVULOSE TEST: CONVALESCENT RHEUMATIC CHILDREN, WITH HEART AFFECTION.

Case No.	Clinical Notes.	Lævulose. Grm.	Percentage of Sugar in the Blood. Fasting.	Hours after lævulose. ½	1	1½	2
12	Rheumatism with transient ht. dis. ..	30	·120	·123	·153	·102	·107
	1 month later (improved)	30	·088	·084	·092	·090	·093
	3 months later (worse)	30	·123	·097	·146	·106	·107
	2 months later (improved).. ..	30	·093	·099	·099	·090	—
13	Rheumatism with persistent ht. dis. ..	30	·076	·107	·162	·127	·122
	1 month later (improving) ..	30	·115	·134	·113	·141	·088
	3 wks. later (improved)	30	·083	·107	·113	·146	·106
14	Sub-ac. rheum. with endocarditis.. ..	30	·088	·120	·165	·116	·097
	3 wks. later (improved)	30	·109	·116	·125	·127	·111
15	Endocarditis following measles	25	·097	·177	·145	·097	·088
	2 wks. later (no change)	25	·106	·148	·180	·166	·157
	3 months later (improved)	25	·093	·106	·130	·127	·095
16	Ac. rheum. with transient ht. dis. ..	25	·102	·113	·115	·123	·106
		25	·102	·102	·111	·100	—
17	Severe rheum. with heart dis.	30	·093	·100	·120	·102	·093
	1 month later (improved) ..	30	·106	·111	·115	·106	·106
18	Severe cardiac rheumatism	25	·099	·138	·145	·169	—
19	Recurrent rheum. with heart lesion ..	30	·100	·196	·177	·162	·159
20	Rheumatic endocarditis	30	·109	·115	·123	·127	·088
	2 months later (improved).. ..	30	·099	·113	·116	·099	—
21	Ac. rheumatic endocarditis	25	·099	·113	·127	·092	·088
	1 month later	25	·109	·164	·115	·093	·088
	3 months later (improved).. ..	25	·097	·100	·109	·097	—
22	Rheumatic endocarditis	25	·077	·092	·125	·111	·093
	1 month later (improving) ..	25	·101	·118	·127	·127	·095
23	Rheumatic endocarditis	25	·116	·118	·120	·138	·099
	3 wks. later (improving)	25	·095	·100	·115	·127	·113
24	Chr. rheum. with endocarditis	25	·106	·109	·141	·123	·109
	1 month later	25	·099	·125	·139	·146	·109
25	Chr. rheum. with endocarditis	25	·127	·090	·102	·116	·090
	1 month later (improving) ..	25	·102	·113	·120	·105	—
	3 wks. later (worse)	25	·102	·127	·143	·139	·120
	1 month later (improved) ..	25	·104	·129	·129	·113	·106

TABLE IV. LÆVULOSE TEST: CHOREIC CHILDREN, WITHOUT HEART LESION.

Case No.	CLINICAL NOTES.	LÆVULOSE. Grm.	PERCENTAGE OF SUGAR IN THE BLOOD. Fasting.	Hours after lævulose. ½	1	1½	2
26	Recent chorea	20	·086	·090	·086	·088	—
27	„ „	25	·084	·086	·084	·097	·083
28	Persistent chorea	30	·094	·113	·100	·090	·083
29	„ „	30	·088	·109	·106	·106	·086

TABLE V. LÆVULOSE TEST: CHOREIC CHILDREN, WITH HEART AFFECTION.

Case No.	CLINICAL NOTES.	LÆVULOSE. Grm.	PERCENTAGE OF SUGAR IN THE BLOOD. Fasting.	Hours after lævulose. ½	1	1½	2
30	Chorea with transient ht. dis.	30	·109	·106	·125	·116	·102
	2 months later (improved).. ..	30	·097	·100	·097	·095	·099
	5 „ „ „	30	?	·107	·107	·107	·097
31	Chorea following sc. fever	30	·088	·104	·115	·122	·090
	2 wks. later (improved)	30	·095	·104	·102	·092	·086
32	Recurrent chorea with endocarditis ..	30	·097	·106	·106	·123	·113
33	Chorea with rheum. pains	30	·106	·127	·180	·162	·125
34	Ac. chorea with rheumatism	25	·093	·120	·125	·109	·102
	1 month later (improved)	25	·093	·090	·088	·088	—
35	Chorea and endocarditis	30	·145	·109	·116	·123	·081
	1 month later (improved) ..	30	·099	·107	·123	·107	·104

COARCTATION OF THE AORTA WITH ULCERATIVE AORTITIS.

BY

F. J. POYNTON, M.D., F.R.C.P.

AND

W. P. H. SHELDON, M.D., M.R.C.P.

(From the Hospital for Sick Children, Great Ormond Street, London.)

Although coarctation of the aorta is a rare condition, a considerable number of examples have from time to time been recorded, and the physical signs to which this deformity of the aorta gives rise form a clinical picture which is often definite enough to enable the diagnosis to be established during life.

Just as congenital defects in the formation of the heart predispose it to infection, so may coarctation of the aorta become complicated by the development of a malignant infective aortitis. Four such instances have already been reported, but because of the rarity of the condition, we feel justified in putting on record the unusual clinical signs and the lesions found at autopsy in the following case. We believe this to be the youngest example that has been reported of infective aortitis complicating coarctation of the aorta.

F. D., a boy aged eight years, was admitted to hospital on October 21st, 1927. Ten days before admission he had complained of feeling unwell. Twenty-four hours later he was feverish and became delirious at night. Throughout these days he complained of pain round his heart, in his chest and in both sides of his "stomach." He was breathless, his bowels were loose, and there were some obscure pains referred to the joints without however any evidence of arthritis.

His previous history threw little light on the diagnosis. His mother volunteered that since he was five years of age he had frequently awakened at night complaining of pains in his knees. He had recently fallen and dislocated his elbow, and had taken the anæsthetic badly for the treatment of this injury, and had never seemed well since that date.

On admission he was obviously very ill and lay in a typhoid state, with a temperature of 103·8° F., pulse 140, and respirations 25 to the minute. The heart was not enlarged. The most important physical sign was a systolic murmur audible at the apex beat, in the left axilla and over the back, but with a maximum intensity to the right of the sternum in the third and fourth intercostal spaces, half way between the sternal edge and the right nipple. There were a few rhonchi in the lungs. The abdomen was tender to light palpation; the liver was felt just below the costal arch, and the spleen, which extended an inch below the costal margin, felt firm and was obviously tender.

There were points in the case which suggested an attack of enteric fever of unusual severity, but the positive signs in the heart favoured the view that there was a septic endocarditis. The bacteriological examinations of the urine and the stools by Dr. D. Nabarro threw more light on the case for they excluded typhoid fever, while the blood after 24 hours grew a pure culture of hæmolytic streptococci.

On the day after admission there was noticed a large pulsating external mammary artery the size of a crow-quill, running down vertically from the right axilla. This artery raised the question of coarctation of the aorta, but no other large arteries were detected elsewhere. There was no sufficient reason to believe there was an aneurysmal dilatation of the vessel in the axilla due to a septic arteritis, for the calibre of the artery was uniform and the only unusual feature was its size.

The condition of the boy was quite hopeless; the temperature remained high, incontinence of urine and fæces supervened, Cheyne Stokes respiration and great restlessness developed, and ultimately death occurred seven days after admission.

Post-mortem examination. The body was wasted, and weighed only 38 lbs. Permission to examine the head was refused.

The heart was slightly enlarged, due to some hypertrophy of the left ventricle. The only other abnormality actually in the heart was the aortic valve, which was bicuspid. The innominate artery and the left common carotid artery had a common origin from the arch of the aorta. The ductus arteriosus was closed. About half an inch beyond the origin of the left subclavian artery, the aorta underwent an abrupt constriction, so that the lumen narrowed down to less than half the original diameter. The constriction extended for only a few millimetres, and immediately beyond the constriction there was a patch of ulceration in the tunica intima about as large as a sixpence. The wall of the aorta at this point was weakened, and bulged slightly. The structures in the posterior mediastinum behind the patch of ulceration were normal and not adherent to the aorta. The abdominal aorta seemed of normal calibre.

Apart from some slight engorgement the lungs were normal. The spleen was enlarged and contained several recent infarcts. Both kidneys contained three or four large recent infarcts. The rest of the body appeared to be normal.

On microscopical examination, nothing was found to indicate the site of the constriction in the aorta. In the area of ulceration, the tunica intima was completely destroyed, and the subintima was swollen and lined on its free surface with masses of streptococci. Clumps of organisms extended down into the tunica media, but became less numerous as the deeper layers were approached. In some of the vasa vasorum masses of streptococci could be discerned. Some of the organisms stained poorly, especially those that could be seen lying within leucocytes.

Summary. In brief, the case is that of a boy aged eight years, who died after an acute illness lasting only 17 days. During this period hæmolytic streptococci were isolated from the blood. Autopsy confirmed the suspicion that there was a coarctation of the aorta, and revealed a patch of ulcerative aortitis just beyond the site of the constriction. In addition, the aortic valve was found to be bicuspid, and there was an abnormal arrangement in the origin of the main arteries from the arch of the aorta.

Discussion.

The subject of coarctation of the aorta has recently been reviewed and brought up to date in a very able article by Maude Abbott in Osler's "Modern Medicine."

Bonnett[1] has divided the condition into two groups. In the first, or infantile group, a diffuse narrowing of the arch of the aorta takes place, and terminates at the insertion of the ductus arteriosus, which is usually patent. The process develops during intra-uterine life, and the examples of this group rarely survive infancy. The second, or adult group, to which our case properly belongs, consists of an abrupt constriction of the lumen of the aorta at or about the level of the insertion of the ductus arteriosus. In some cases complete obliteration of the lumen has been found.

There is a striking predominance of the condition in males; in 146 examples of the adult type, Abbott found that 102 were males.

Although grave anomalies in the formation of the heart and large vessels are more frequently associated with the infantile than the adult type, in the latter group certain minor defects are relatively common, and the most usual of these are bicuspid aortic valves and variations in the origin of the great vessels.

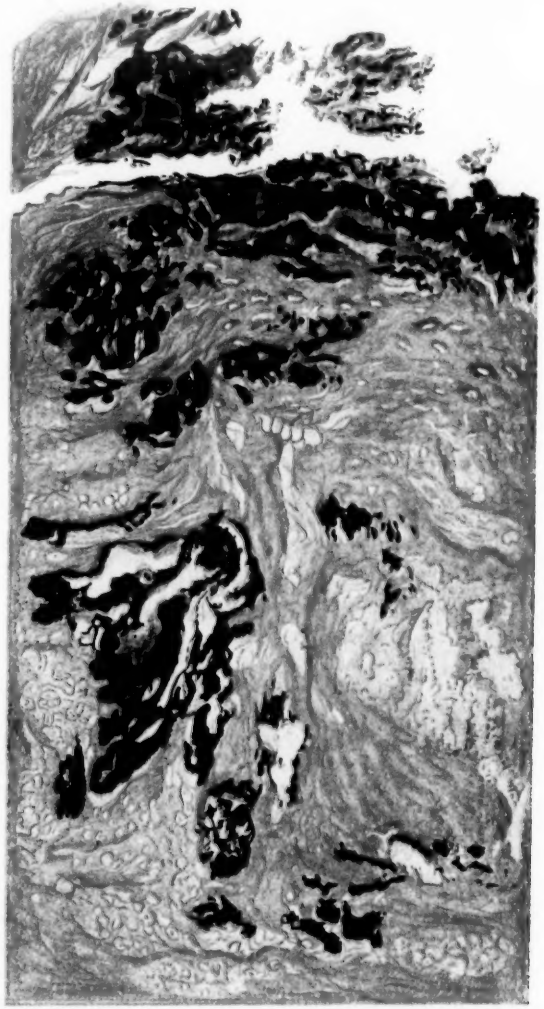

FIG. 2.—Microscopical section of aorta through the edge of the area of ulceration. The ulcer is lined by masses of organisms (stained blue), and these have penetrated into the tunica media, tending to occupy the vascular spaces. Stain : Nile blue and van Gieson. 2/3 objective.

FIG. 1.—Natural size illustration of specimen of coarctation of the aorta. Immediately beyond the point of constriction is an area of ulcerative aortitis. In addition, there is some hypertrophy of the left ventricle, the aortic valve is bicuspid and the innominate and left common carotid arteries arise from the aorta by a common trunk.

Abbott points out the unusual position of the murmurs that have been described and draws attention to the remarkable latency of any symptoms or signs in many cases of coarctation until some disaster, such as has been described here, has supervened. In some cases, presumably those in which a sufficient anastomosis of vessels between the upper and lower portions of the trunk is rapidly and easily formed, coarctation of the aorta may have no effect upon the length of life. The condition has been found at autopsy on a man aged ninety-two. In others, death is brought about through a gradual failure of the left ventricle.

Termination by infective aortitis is quite unusual, and a brief analysis of the recorded cases will therefore be given.

Case 1. (Focken.[2]) Male aged 20 years. Coarctation at the level of the obliterated ductus arteriosus. The aorta just beyond the constriction was the site of ulceration. Vegetations were present here and on the aortic valve, which was bicuspid. Streptococcus viridans was isolated from the blood.

Case 2. (Focken.[2]) Female aged 18 years. Coarctation just beyond the insertion of the obliterated ductus arteriosus. Immediately below the constriction was an aneurysmal dilatation of the aortic wall, due to a small patch of ulcerative aortitis. The aortic valve was bicuspid. A blood culture before death grew hæmolytic streptococci.

Case 3. (Smith and Hausmann.[3]) Male aged 17 years. Coarctation was in this case also associated with a bicuspid aortic valve. There were vegetations on the aortic and mitral valves, and one centimetre below the constriction of the aorta a small saccular aneurysm had formed, and had ruptured into the left pleura. Streptococcus viridans was isolated from the blood.

Case 4. (Reifenstein.[4]) Male aged 10 years. Coarctation of the aorta 2·5 cm. below the origin of the left subclavian artery. Immediately below the constriction a saccular aneurysm had formed, and had burst into the œsophagus. The arteritis was in this case pneumococcal in origin.

An interesting feature of all these cases is that the infection of the aorta occurred at a level just beyond the point of coarctation.

The cause of this deformity of the aorta is unknown. It has been suggested (Skoda) that there is an extension of the tissue of the ductus arteriosus into the wall of the aorta. When the ductus undergoes contraction after birth, the same change takes place in the tissue in the wall of the aorta, and gives rise to coarctation. This view receives some support from the fact that the condition has never been found in the fœtus nor until several weeks after birth, and in addition the ductus arteriosus is found obliterated in over 90 per cent. of cases, whereas in the infantile type the ductus is usually patent. On the other hand the constriction is not necessarily at the level of the entrance of the ductus arteriosus, but, as in our case, may be definitely below this level.

REFERENCES.

1. Bonnet, L. M., *Rév. de Med.*, Paris, 1903, XXIII, 481.
2. Focken, E., *Ztschr. f. klin. Med.*, Berlin, 1924, C, 179.
3. Smith and Hausmann, *Arch. Int. Med.*, Chicago, 1926, XXXVIII, 367.
4. Reifenstein, *Am. J. Med. Sc.*, Philad., 1924, CLXVIII, 381.

ON LOBULAR AND LOBAR PNEUMONIA IN INFANCY AND CHILDHOOD.

BY

OLIVE SOMERVILLE, M.B.,

Muirhead Scholar.

(From the Medical and Pathological Departments of the Royal Hospital for Sick Children, Glasgow.)

Although much has been written and many statistical studies published on the relative frequency and age incidences of the different types of pneumonia in childhood, anything but unanimity prevails. This diversity of opinion is most marked regarding pneumonia as it occurs during infancy and early childhood, and is undoubtedly dependent on the different criteria which the individual workers have adopted for the differentiation of the lobar and lobular types of the disease. Some observers have based their classification on clinical grounds, believing that a definite diagnosis is possible from the history of the illness, the physical signs, the type of fever and degree of toxæmia present. This is a belief, however, which in our experience is not substantiated by the pathological findings. Others[1] lay stress on the type of shadow revealed on the fluoroscope which they state is characteristic for each type of the disease. Others again have used a bacteriological basis of classification, while a small minority have employed the anatomical characters of the lesion as found at autopsy.

As in our opinion it is only on the basis of the anatomical nature of the lesion that any reliable decision on the matter can be reached, and as only relatively few of the previous studies of this question have been of this nature, we decided to investigate the subject from this point of view and the present communication is a record of the results obtained.

Material and Methods. The material investigated consisted of all the acute pneumonic conditions examined post-mortem in the Royal Hospital for Sick Children, Glasgow, from January 1925 to June 1926, and amounted in all to 65 cases. Pieces of tissue were taken from the various lobes of the lungs and were fixed in (1) ten per cent. formalin solution, (2) Zenker's solution, and (3) a saturated solution of bi-chloride of mercury. Paraffin sections, generally about a square inch in size, were stained with (1) Harris's hæmatoxylin and eosin; (2) Gallego's modification of Mallory's method[2]; (3) Weigert's fibrin stain[3]; (4) Iron hæmatoxylin; (5) Methylene blue and eosin.

Anatomical Features of Various Types of Pneumonia.

Anatomically the chief distinguishing features of each type may be summarized as follow. Lobar pneumonia spreads by direct continuity of ung tissue and leads to massive consolidation with a lobar distribution; the

disease may spread more widely until it involves almost the whole lung, but it is not common to find two separate areas in the same lung. Broncho-pneumonia, on the other hand, shows a patchy distribution, with lesions widespread throughout both lungs, though one lung may be much more affected than the other: an entire lobe is rarely consolidated.

The histological picture in lobar pneumonia is fairly constant. The chief feature is the abundant exudate of fibrin and polymorphs into the alveoli, septa, and the bronchioles. There is universal involvement of every portion of the lobe and of the different structures in the lobe. In spite of this intense inflammatory affection of the lung, there is, in the acute stage of the lobar type, very little cellular infiltration of the interstitial tissue in contrast to the marked interstitial changes in broncho-pneumonia. This has been pointed out by McCallum[4] as a striking and distinctive feature in which the two forms differ.

The picture in broncho-pneumonia is more complex, but on section of the lung, the lobular distribution of the lesion can usually be made out, patches of dense leucocytic exudate being found in relation to the bronchioles and infundibular passages. The margins of the consolidated areas are ill-defined, irregular in outline, and separated by healthy, collapsed or emphysematous lung. The abundant fibrin formation, so constant in the lobar variety, does not occur. Some fibrin, however, is seen occasionally in the alveoli immediately surrounding the affected bronchioles, and this is said[5] to be found more often in the influenzal than in any other form. The inflammation is largely catarrhal in nature with a few polymorphonuclear cells, though in some cases polymorphs are the predominating cellular elements. As previously noted, the interstitial tissue is always markedly affected, being infiltrated with large numbers of cells.[5, 6]

Although in typical cases the histological features of the two forms are quite distinct, many intermediate forms, which partake of the characters of both, are recognized. In such cases the points to be relied upon for diagnosis are (1) the nature of the exudate, (2) the implication of the interstitium, and (3) the mode of spread as evidenced by a patchy cellular reaction.

Results.

From the study of the morbid anatomy and histology in conjunction with the clinical histories, which were employed to separate the primary from the secondary forms, the 65 cases have been classified as follows:

I. Broncho-pneumonia:

(1) *Primary broncho-pneumonia*, in which the onset was either sudden or gradual in a previously healthy child: this group includes some cases with a clinical history indistinguishable from lobar pneumonia but in which lobular lesions were found on pathological examination.

(2) *Secondary broncho-pneumonia*, in which the pneumonia followed on some preceding disease, such as (*a*) infectious fevers, disease of of respiratory passages (*e.g.*, bronchitis), urinary tract, or nervous

system; (*b*) chronic disease or malnutrition, *e.g.*, marasmus, pyloric stenosis, syphilis, tuberculosis, congenital disease of the heart, tetany, rickets, and gastro-enteritis; and (*c*) following operations.

(3) *Influenzal broncho-pneumonia.*

II. Lobar Pneumonia.

The relative number of the different types and the age distribution from the findings in 65 cases are given in Table I.

Table I.

Showing Age Incidence of Cases Examined Histologically.

Age in Years.	0—1	1—2	2—3	3—4	4—5	5—6	Total
Primary broncho-pneumonia	22	8	3				33
Secondary broncho-pneumonia ..	10	5	2	1			18
Influenzal broncho-pneumonia ..	6	2		2		1	11
Lobar pneumonia		1				1	2
Mixed lobar and broncho-pneumonia			1				1
	38	16	6	3		2	65

(1) Primary Pneumonia.

Under this heading primary broncho-pneumonia and lobar pneumonia will be discussed together, as most difficulty was found in the differentiation of these two forms. Thirty-six cases were examined, thirty-three of these being lobular in type, two lobar, and one mixed. Excepting one of the cases of lobar pneumonia, all occurred in children below three years of age. Of the thirty-three lobular forms, seventeen were diffuse and in three cases closely simulated lobar pneumonia; the remaining sixteen showed typical lobular lesions.

On microscopical examination of all the cases of broncho-pneumonia, the lobular distribution could be made out at some part. In many cases by the aggregation of foci the consolidation had spread through almost an entire lobe, giving the appearance of hepatization, but the microscopical features were more of the lobular type, areas of emphysema being intermingled with densely cellular areas, and typical lobular lesions were found in other lobes.

The commonest lesions were those of a pneumonia of about two weeks' duration, and the conditions found in such circumstances will first be described. The bronchi showed desquamation of epithelium varying in degree in different parts of the same section, but seldom as severe as in the smaller bronchioles. Their lumina were plugged with a cellular exudate of polymorphs and desquamated epithelial cells, the latter often in plaques, with a few red blood cells and small round cells. The bronchial walls were congested and often

infiltrated with numbers of small round cells. According to Gaskell,[7] this lymphocytic peribronchial reaction varies directly with the virulence of the infecting organism. There was less desquamation of the lining epithelium of the bronchi than of the bronchioles, some parts generally remaining covered with normal epithelium. Sometimes, in the smaller bronchi, only a thin layer of polymorphonuclear and epithelial cells was to be seen on the top of the basement membrane lining the lumen. In a few of the diffuse types, fibrin was found extending through the walls into the air vesicles immediately surrounding some of the more severely affected bronchi.

The desquamation of the lining epithelium of the bronchioles in the consolidated areas was always severe, the walls being either partially or completely denuded. A densely cellular exudate of polymorphs and desquamated epithelial cells completely filled the lumen, the polymorphonuclear exudate extending directly into the alveoli through the infundibular passages. Definite suppurative change was found in 35 per cent. of the cases: in these the basement membrane showed a break in continuity and polymorphonuclear cells were invading the surrounding lung tissue. In more than half of the cases lymphocytic reaction was present round the bronchioles: this was very marked in nine cases in which several aggregations of small, round cells were seen in the walls. In the lobular forms no fibrin was present, but some of the diffuse types showed a little extending through the bronchiole walls into the adjacent alveoli.

The air vesicles round the affected bronchi and bronchioles were consolidated in an irregular, patchy manner. In the lobular forms, the areas of consolidation were small, and in the centre of each, one or more plugged bronchus or bronchiole could be distinguished, and the alveoli surrounding the patch were emphysematous. The diffuse types, however, showed widespread consolidation, and in some sections no unaffected alveoli could be seen, as the patches had completely merged into one another. The cellular exudate was in twenty-one cases mainly polymorphonuclear, but in the remaining twelve cases small round cells and catarrhal cells predominated. In several cases it was noted that the exudate in the bronchioles was wholly polymorphonuclear, and the cell reaction in the alveoli consisted of mononuclear cells.

The density of the consolidation always varied considerably in different parts: some alveoli were packed tightly with a mass of polymorphonuclear; some contained mucoid and granular material with only a few cells in various stages of disintegration; and others contained chiefly large mononuclear cells. The cellular exudate was always more abundant in the air vesicles immediately surrounding the bronchial passages than in those at the margin of the patch; and sometimes definite zones of inflammation could be made out resembling successive stages of lobar pneumonia, these being from within outwards (1) grey hepatization, (2) early red hepatization, and (3) primary catarrhal stages.[7] Areas of œdema with hæmorrhage were occasionally seen, but these were both more common in the influenzal forms. Interspersed among the affected areas were emphysematous alveoli or single distended air vesicles in which no exudate

was present. Small areas of collapse were often found round the terminal bronchioles, at the margin of the consolidation, or, as described by Armstrong and Gaskell,[8] under the pleural surface.

The interstitial tissue was invariably affected to a greater or lower degree, depending on the extent of the lesion. The alveolar walls were swollen and infiltrated with cells, sometimes thereby encroaching on the alveolar spaces to a marked degree. In the more advanced stages where suppurative change had taken place the walls of the air vesicles were indistinguishable, and masses of polymorphonuclear, with a broken down bronchiole in the centre, were all that remained. In several cases the interstitial tissue between the lobules, and in the neighbourhood of the bronchi and vessels, was increased in size on account of infiltration with polymorphonuclear and deposit of fibrin.

A slight fibrinous layer was found on the pleura where the consolidation had reached the surface of the lung, but extensive pleurisy such as is usually seen in lobar pneumonia was never present. Pneumococci were invariably found in the pus from the finer bronchi, seldom in pure culture, but generally mixed with streptococci, pneumobacilli, and occasionally also with staphylococci.

The above description applies to all types of primary broncho-pneumonia encountered. In sixteen cases the lobular distribution was easily recognized both macroscopically and microscopically, and the clinical history was also typical of that form of the disease. In the eighteen remaining cases of lobular pneumonia and in one of the lobar cases, more difficulty was found in differentiation, and prolonged histological examination was necessary before they could be finally classified. Fourteen of these showed the characteristics of a lobular lesion which, by fusion of adjacent foci of consolidation, involved the greater part of one lobe, and so simulated lobar pneumonia on naked-eye examination. Histologically, however, cellular reaction was found to be most intense round the bronchi, the exudate being irregular in density and nature, parts of the same lung showing a polymorphonuclear exudate, whilst in other parts large mononuclear cells predominated. Fibrin was scanty, being found in only six cases and always confined to the air vesicles immediately surrounding the bronchioles.

The remaining five cases showed features of both lobar and lobular types and the following summary of each case will demonstrate the difficulties encountered in arriving at a satisfactory conclusion regarding these forms.

Case 1. Boy, aged 1 year, 10 months. He was drowsy and off food for about one week before the onset of cough and dyspnœa. Two days later he had a rigor. His symptoms increased in severity until, three days later, he was admitted to hospital where he died twenty-six days afterwards. During this time, the physical signs of pneumonia were limited to the base of the left lung. The temperature was irregular, between 99° and 103°F., and the pulse and respiration rates were correspondingly high. The leucocytes numbered 28,000 per c. mm.

At the autopsy, there was found a diffuse consolidation of the entire left lower lobe, apparently of lobar type and in the stage of red hepatization, the other lobes being unaffected. Fibrinous pleurisy and early pneumococcal pericarditis were also present. On histological

examination the consolidation was found to be loose and fairly uniform, cells were polymorphonuclear and mononuclear, but the reaction was most intense around the bronchioles, fibrin was absent, and there were occasional unaffected alveoli. The pneumococcus alone was found on culture of the pus from the smaller bronchi.

In this case the symptomatology was atypical, and the physical signs and naked-eye post-mortem findings were those of lobar pneumonia. It was only on histological examination that it was possible to make out the lobular nature of the lesion.

Recovery would probably have taken place if the additional burden of pericardial infection had not supervened in a child already worn out by a long continued fever, and the case would have been classified as one of lobar pneumonia.

Case 2. Girl, aged 1 year, 2 months. Since bronchitis at eight months she had never been well. Ten days before admission, cough and heavy breathing developed, and gradually increased in severity. On admission the child was very ill with physical signs of pneumonia of the entire right lung and the left apex; the condition remained unchanged till death eight days later. The temperature was persistently high, and the pulse and respiration rates correspondingly increased. The leucocytes were 97,600 per c. mm. on admission.

At the autopsy, a diffuse lesion was found involving almost the entire right lung with the exception, in each of the lobes, of a small portion of the anterior edge which was the seat of acute vesicular emphysema. The line of demarcation between the consolidated area, which resembled the grey stage of a lobar pneumonia, and the emphysematous area was very irregular, the one passing imperceptibly into the other. Fibrinous pleurisy was present over the surface of the right lung. The left upper lobe was the seat of typical lobular lesions. Histologically, the most notable features were the abundant fibrinous exudate extending throughout the alveoli, and the marked peribronchial polymorphonuclear reaction. The interstitial tissue was affected to a considerable extent, being infiltrated with fibrin and large numbers of polymorphonuclear cells.

Clinically this case showed many of the features of lobar pneumonia in the severity of the general symptoms and the maintenance of high fever throughout its course, but the mode of onset and the physical signs were more of the broncho-pneumonic type. The lesion in the right lung resembled in some respects a lobar pneumonia on naked-eye examination, but the histological changes, though somewhat atypical on account of the large amount of fibrinous exudate, were more of the nature of a lobular form of infection, and the fact that a definite broncho-pneumonic consolidation was present in the other lung gave additional support to this conclusion.

Case 3. Girl, aged 2½ years. The symptomatology was that of a pneumonia of fairly acute onset and course; death taking place after an illness lasting three weeks. The following lesions were found at the post-mortem examination: (1) consolidation of the entire right lower lobe, with collapse of right upper and middle lobes; (2) large right-sided empyema; (3) slight pericarditis; (4) bilateral otitis media. On histological examination of portions of the affected lung, a mixed type of lesion, in many respects resembling lobar pneumonia, was found. There was diffuse consolidation of the air spaces with much fibrinous exudate, but cells, though numerous in the bronchi, were scanty in the air vesicles and were mainly mononuclear in type. The desquamation of the lining epithelium of the bronchi and bronchioles was almost complete, their lumina being plugged with dense collections of polymorphonuclear cells with marked degenerative changes in their nuclei. The exudate in the bronchioles was observed to be directly continuous with that in the air vesicles. Peribronchial lymphocytic reaction was very marked. No areas of emphysema, collapse, œdema, or hæmorrhage were present in the sections examined, but there was much suppurative change of a characteristic lobular type.

In this case an entire lobe was affected. The lesion was associated with empyema, a fact thought by Still[9] to be almost pathognomonic of co-existing lobar pneumonia, and the exudate was largely fibrinous in nature. All these points were in favour of a lobar lesion, yet the

histological features, especially the secondary suppurative change, were more characteristic of broncho-pneumonia. Such an intense affection of the air passages and so marked a peribronchial reaction are never found in a lobar pneumonia.

Case 4. Boy, aged 2 years. The illness began with diarrhœa and was followed two weeks afterwards by cough, fever, and rapid breathing. He was admitted to hospital one week subsequently when the symptoms had increased in severity, with the physical signs of a right-sided pneumonia. Death occurred three weeks later.

At the autopsy, a diffuse, uniform consolidation, granular in appearance and suggesting red hepatization, was found to involve the entire right upper lobe, although the middle and lower lobes showed typical lobular lesions. There was fibrinous pleurisy on the surface of the right lung. The left lung was normal in appearance. Sections of the right upper lobe showed in the air vesicles a diffuse exudate of fibrin with polymorphonuclear and small round cells. The desquamation of the epithelium of the bronchi and bronchioles was not severe, and all were affected more or less to the same degree. Peribronchial lymphocytic reaction was slight, the interstitium was practically unaffected, and there were few catarrhal cells and no areas of emphysema or collapse. The pneumococcus alone was found in the pus from the smaller bronchi. The lesions in the other lobes were typically lobular in type.

The lesion in the right upper lobe in this case was characteristically lobar in distribution, in its post-mortem appearances, and its histology, though the symptomatology was not typical of this disease. The fact that lobular lesions were present in other lobes may account for the atypical course of the illness.

Case 5. This case, though lobar in type, showed many atypical features and will be described briefly to compare with the above four cases.

Boy, aged 1 year. He was admitted to hospital moribund, with the history of fever and heavy breathing of three weeks' duration. There was severe anæmia: hæmoglobin, 10 per cent.; red cells, 2,500,000; and leucocytes, 2,000 per c. mm. He died a few hours after admission.

At the autopsy extensive consolidation, greyish and uniform in distribution, was found involving the entire right upper lobe and the lateral part of the middle lobe, the rest of the lungs being unaffected. Associated with this were left acute otitis media, and longitudinal sinus thrombosis with meningeal hæmorrhage. On histological examination of portions of the lung involved, a very diffuse, fairly uniform consolidation was found, and an exudate composed of polymorphonuclear cells and much fibrin. In some parts the exudate had retracted from the alveolar walls. The desquamation in the bronchioles was only moderately severe, but there was marked peribronchial lymphocytic reaction. Many large mononuclear cells were present in some parts. There was slight cellular infiltration of the interstitial tissue and there were no areas of emphysema, collapse, or hæmorrhage.

This case, though showing a few of the features of broncho-pneumonia, namely, the peribronchial lymphocytic reaction, was certainly more of a lobar type of consolidation as the fibrinous exudate was uniform in distribution. The air passages, too, were less involved than would be expected in such a severe broncho-pneumonic infection, and the interstitium was practically unchanged. In addition, it is very unusual to find the other lobes of the lungs unaffected in a severe confluent form of broncho-pneumonia. The conclusion was therefore drawn that this was a lobar pneumonia.

Both clinical and post-mortem findings did not correspond to the classical types in all five cases. In each case one lobe at least was consolidated in its entirety, thus simulating the stage of red or grey hepatization of a lobar pneumonia, and in only two cases was there any lobular consolidation in other parts. The only naked-eye characteristics pointing to the lobular nature of

the lesion were the irregular margins of consolidation in Case II and the type of suppuration in Case III.

Even the histological findings were by no means typical. Four cases showed such an abundant fibrinous exudate as is rarely found in acute bronchopneumonia, and no areas of emphysema or collapse were found in the consolidated area. The first three cases were distinguished as lobular in type, the significant features being, first, the evidence of bronchial spread from the marked affection of the air passages and intense peribronchial reaction, and secondly, the affection of the interstitium. The fourth case showed lobar and lobular lesions, and the fifth was lobar in nature, though atypical in some of its features.

These five cases represent very different forms of pneumococcal infection and illustrate some of the difficulties encountered in reaching a correct classification even after careful histological examination. A feature common to all was the occurrence of the disease in the second or third year of life. In the cases occurring during the first year and after the third year there was never any doubt regarding the nature of the lesion; it was only those cases occurring during the intervening period (second and third years) which presented difficulties in classification. It might be inferred from this fact that a transition takes place at this time, the pneumonia gradually losing its lobular character and approaching the lobar form of the adult. In support of this view may be quoted the opinion of M. Valleix[10], who, as early as 1850, described similar differences according to age. He divided the cases into three periods: (1) up to two years, (2) two to six years, and (3) six to fifteen years, and regarded the second period as one of transition from the invariable lobular form of the first period to the lobar form of the third; the fatality of the disease was found to diminish correspondingly.

To compare with these mixed forms, details of the only case of typical lobar pneumonia in the whole series are appended.

Case 6. Boy, aged 5 years. The history was that of an acute illness of three weeks' duration, with marked general symptoms, high fever, and definite physical signs of consolidation of the right lung.

At post-mortem examination, complete consolidation of the right lung was found with a localized empyema, slight pericarditis, bilateral acute otitis media, and pneumococcal meningitis: the left lung was unaffected. Sections of the right lung showed extensive fibrinous consolidation of uniform density. The cells were chiefly polymorphonuclear showing much fragmentation of nuclei. There was present fairly severe catarrh of the bronchioles, and to a lesser degree of the bronchi, with marked peribronchial infiltration by small, round cells; but there was not much variation in the degree of change, and no free alveoli. There was some early diffuse suppurative change. The interstitium was practically unaffected; there were no areas of catarrhal inflammation and no collapse. The pneumococcus, staphylococcus, and pneumobacillus were all found in pus from the fine bronchi; and the pneumococcus was found in the pus from the surface of the brain, and from both middle ears.

The great differences between this case and those previously cited were the uniformity of the lesion, the slighter degree of affection of the bronchioles

and interstitium, and the absence of catarrhal inflammation. In this case, also, the clinical and post-mortem features agreed, and were typical of the lobar form of the disease.

(2). Secondary Broncho-Pneumonia.

In the examples of secondary pneumonia, the pathological picture was more constant and conformed fairly closely to the typical lobular form already described. Seventeen of the total eighteen cases were of this type. The lesions were of a patchy distribution, affecting both lungs in more than half of the cases, and often being at a more advanced stage in the posterior parts of the lower lobes. Microscopically, the chief features were the lobular distribution of the consolidation, with marked affection of the bronchi and bronchioles, and areas of emphysema and collapse. Fibrin was usually absent, and œdema and hæmorrhage frequently occurred. In eleven cases the cellular exudate consisted of polymorphonuclears and mononuclears, though polymorphonuclears were more abundant in the bronchi; in the other seven cases polymorphonuclears predominated throughout the consolidated area. Peribronchial lymphocytic reaction was very marked in one-half of the cases; clumps of small, round cells being present in the walls of the bronchi and vessels. Catarrhal cells were found in large numbers in all cases. Suppuration was the exception. Pleurisy only occurred in two of the cases when there was a scanty deposit of fibrin on the pleural surface.

In only one case did the infection show any tendency to spread through an entire lobe in a diffuse manner. Here the condition was secondary to a sub-acute nephritis.

Case 7. Girl, aged 3¾ years. The history was of generalized œdema of two week's duration with the development of cough, fever, and rapid breathing one week before death. The lungs showed a diffuse consolidation of all the lobes with much hypostatic congestion, œdema, and some hypostatic pneumonia. There was a little clear fluid in both pleural sacs. A definite sub-acute nephritis was present.

Sections of portions of the lung showed a diffuse fibrinous consolidation, loose and irregular in density, with intense peribronchial lymphocytic reaction, and practically complete desquamation of the epithelium of the bronchioles. A dense polymorphonuclear exudate, continuous with that in the air vesicles, was present in the bronchioles; and in places the walls of the air vesicles showed breaking down on account of suppurative change. In some regions there were numbers of round and large mononuclear cells. No areas of collapse were seen, and none of hæmorrhage.

Though this case showed a lobar distribution, the histological features were those of a lobular pneumonia with aggregation of adjacent foci of consolidation, œdema being present in the intervening areas. The diagnosis by microscopical examination presented very little difficulty.

(3). Influenzal Broncho-Pneumonia.

The lesions most often found in the influenzal forms of pneumonia were similar to those of a diffuse primary broncho-pneumonia of a very severe type. Eleven cases were examined and in all of these a bacillus corresponding to Pfeiffer's influenzal bacillus was isolated from the pus in the finer bronchioles;

in the larger bronchi, pneumococci and streptococci were also present. Eight of the cases occurred in the first two years of life, two in the fourth year, and one in the sixth year (see Table I). The duration of the illness was in all cases less than three weeks, in six being under one week. Extensive lesions were found in both lungs ; in seven cases every lobe was affected, and in the remaining four cases foci were present in both lower lobes. In six of the cases on naked-eye examination there was diffuse consolidation of the lower portion of a lower lobe simulating red hepatization, but the upper margin was irregular and showed a less advanced stage of consolidation. Emphysema was always marked in the free parts, much more so than in any other form of pneumonia. Microscopically, the consolidation was invariably bronchial in distribution and cellular in nature ; fibrin, when present, was confined to the air vesicles in immediate relation to the bronchi. Bronchitis and bronchiolitis were severe, and in most cases suppuration had occurred. In the types which showed lobular consolidation on naked-eye examination, and in the less advanced parts of the diffuse forms, both polymorphonuclear and mononuclear cells were present, fibrin was scanty, and the consolidated areas, which varied in size, always surrounded a bronchiole and were separated from one another by areas of compensatory emphysema. In the diffuse forms, the consolidation still retained its lobular character ; both mononuclears and polymorphonuclears were present but more numerous in the suppurative areas, in the lumina of the bronchi and bronchioles. There were many areas of hæmorrhage and collapse. Peribronchial lymphocytic reaction was only slight. Large mononuclear cells were present in all cases but were scanty. Pleurisy was only present in three cases.

Conclusions.

From this study of the histology of pneumonia it is evident that broncho-pneumonia is the typical lesion of infancy and early childhood, and is the invariable type in the secondary and influenzal forms. It may be concluded, also, that lobar pneumonia, although it does occur, is the exception during the first three years of life, and never takes the typical form of the same disease as found in the adult. During this period, however, certain mixed forms with many of the characteristic features of lobar pneumonia do occur, and can only be distinguished by a careful histological examination. To this end, the simplest and most conclusive method would be by making histological sections of the entire lung, for this would show the mode of spread of the inflammatory process and the extent of the lesion. In the present investigation, the means available did not allow of large sections being made. These mixed forms occur most frequently during the second and third years of life. After the age of three years, the disease is more often lobar in type though it would appear from the post-mortem records that this lesion is occasionally associated with broncho-pneumonia. If the latter does occur alone after three years of age, it is usually either secondary or influenzal ; in the few cases in which it is primary, it occurs in an atypical form.

It is difficult to find an explanation of this variation in the character of the lesions in the earlier years of life. Gaskell, in his experimental work on

rabbits, found great difficulty in producing lobar lesions and suggests that the size of the lung may be of some importance, the larger lung of the adult allowing time for concentration of the inflammatory reaction and therefore being more favourable for keeping the infection within the lobe. It has also been suggested that lobar pneumonia is always a pure pneumococcal infection, whilst in broncho-pneumonia a mixed infection is the rule, but this is not invariably so. In some cases of primary broncho-pneumonia, the pneumococcus alone is found, and on the other hand, a few cases of lobar pneumonia show a mixed bacterial flora.

Whatever the explanation, it would seem quite definite that the cause of the variation in the type of reaction is some inherent tendency in the child. This may be dependent either on some peculiarity of the lung itself or in consequence of some subtle serological or metabolic characteristic associated with the period of life. We are quite familiar with the varying susceptibility of different organs to a specific organism, e.g. the meningococcus; with the varying susceptibility at different age periods of any individual organ to a specific organism, e.g. rheumatic infection; with the varying type of reaction at different ages to a specific organism, e.g. tubercle bacillus; and with the varying susceptibility of an organ to an infection which occurs under special or unusual circumstances. Of the last phenomenon the immunity of the cerebrum to the Treponema pallidum in a person subject to malaria may be cited.

It thus seems possible that some subtle metabolic characteristic may bring about a special pulmonary reaction in response to infection with the pneumococcus. In this way there could be explained the different reactions in the infant and adult and also the mixed type of reaction which occurs during the stage of transition from the characters of the infant to those of the adult.

Summary.

1. Sixty-five cases of pneumonia were examined by histological methods and a bacteriological examination was made in some of these.

2. Only one case of typical lobar pneumonia was found, this being in a boy of five years, but two atypical lobar forms were found in children of one and two years and in one of these there was, in addition, a lobular lesion in the other lung.

3. Of thirty-five cases of acute primary pneumonia examined, sixteen showed typical lobular lesions, fourteen were diffuse with a lobar distribution in one lobe, but easily differentiated on microscopical examination; the remaining five were mixed types with features of both lobar and lobular forms and these occurred in the second and third years of life.

4. In the eighteen secondary cases, the lesions were typically lobular in distribution and in their histological features.

5. The influenzal cases showed characteristics of an intensely virulent infection. The lungs were extensively involved, six of the eleven cases showing almost a lobar distribution, but the consolidation was always lobular in nature.

6. Pure pneumococcal infections occurred in both lobar pneumonia and primary broncho-pneumonia, but in many cases, the pneumobacillus, streptococcus and staphylococcus were also found, and in secondary and influenzal forms a mixed infection was invariable.

REFERENCES.

1. Armand-Delille, P. F., *Brit. Med. J.*, Lond., 1927, ii, 588.
2. *Med. Sc., Abs. & Rev.*, Oxf., 1925, XI, 43.
3. Green's, *Pathology*, Lond., 1923.
4. MacCallum, W. G., *Textbook of Path.*, Lond., 1923.
5. Muir, R., *Textbook of Path.*, Lond., 1924.
6. Wollstein, M., & Goldbloom, A., *Am. J. Dis. Child.*, Chic., 1919, XVII, 165.
7. Gaskell, J. F., *J. Path. & Bact.*, Edin., 1925, XXVIII, 427.
8. Armstrong, R. R., & Gaskell, J. F., *Ibid.*, 1921, XXIV, 369.
9. Still, G. F., *Com. Dis. & Disorders of Child.*, Lond., 1924.
10. Valleix, M., *Am. J. Med. Sc.*, Philad., 1850, XIX, 211.

ARSENIC IN THE TREATMENT OF CHOREA.

BY

STANLEY GRAHAM, M.D.,

(From the Medical Department, Royal Hospital for Sick Children, Glasgow.)

Arsenic has been used in the treatment of chorea for more than a century with results which are generally considered to have established its usefulness. In 1918, Osler[1] stated that " with the exception of arsenic no remedy seems to have any influence in controlling the progress of the affection." There would seem, however, to prevail great difference of opinion regarding the dosage, some authors recommending large doses and others small.

In 1813 Martin[2], when he originally suggested the use of the drug, advised starting with a dose of five minims of Fowler's solution thrice daily, and increasing the dose by one minim daily until signs of intolerance appeared, when it should be stopped. Murray[3], in 1899, recommended large doses from the beginning, namely, fifteen minims thrice daily, to be continued for a week. Jacobi[4], who also favoured large doses, believed that the cause of failure on the part of arsenic could generally be ascribed to insufficient dosage. In marked contrast to these views is that expressed by Langmead[5] in 1913 who said that arsenic should not be employed because of the bad effects often seen.

It is generally admitted that one of the serious disadvantages to the use of arsenic by mouth is the tendency of the drug to cause vomiting. Hence the administration by the subcutaneous route has been occasionally carried out. Radcliffe[6] must have been one of the first to practice this method which he described in Reynold's System of Medicine in 1872. This route of administration has the great drawback that it causes considerable local irritation and thus was found to be unsuitable for children.

With the advent of the organic arsenical preparations, and the possibility of their introduction by the intravenous route, it was only natural that they should be employed in the treatment of chorea in the hope that, in this way, local irritation could be avoided and at the same time much larger amounts of arsenic safely given. Many authors have reported examples of chorea treated by arsenic intravenously. Bokay[7], in Budapest, has probably been the most enthusiastic supporter of the method which he first recommended in 1911. Recently[8] he has again expressed his views in its favour, and records two cases in which the chorea had been present, in one for five weeks and in the other for four weeks ; in these, after the administration of 1·2 grm. and 1·5 grm. of neo-salvarsan, all movements disappeared in forty-three and thirty-three days respectively. In his original paper he gives no figures relative to results, and quotes only one case. In this patient the chorea had been in existence for one year, and disappeared in thirty-five days after the injection of

1·2 grm. of salvarsan. Moffett and Smith[9] have still more recently commented on the treatment of nine cases with sulpharsphenamine, but merely state that in five definite clinical improvement resulted.

Present Investigations.

Reference to all the available records reveals wonderfully scant evidence of the value of arsenic intravenously in the treatment of chorea, and a complete absence of any actual comparison with cases treated by other methods. Since impressions are notoriously apt to be erroneous, it was deemed advisable to compare two series of cases treated synchronously, one with arsenic intravenously and the other with arsenic by the mouth. There is included for comparison a similar number treated by sodium salicylate though not during the same period. The arsenic was given intravenously in the form of neo-kharsivan at four-day intervals, and by the mouth as Fowler's solution in fifteen minim doses, thrice daily. In each case the drug was continued until all choreiform movements disappeared or until toxic signs supervened. The sodium salicylate was given in ten to twenty grain doses, with twice the amount of sodium bicarbonate, five times daily. Treatment was begun immediately after admission of the patient to hospital. The cases were not selected in any way, and other therapeutic factors were common to all groups, the patients being confined to bed in the recumbent position and receiving full hospital diet.

The average amount of neo-kharsivan administered was 2·15 grm. (containing 0·465 grm. arsenic), three cases being given 3·15 grm., 3·6 grm. and 3·9 grm. each within a period of thirty days. In four of the cases signs of intolerance in the form of a skin rash appeared, but in only one of these was it severe. These toxic symptoms did not occur in any of those cases receiving the largest doses, a fact which supports the usual teaching that the size of the dose *per se* is not responsible for such manifestations, but rather some idiosyncrasy on the part of the patient. Of the fifteen cases treated, ten had cardiac murmurs on admission, and ten on dismissal three months later. In two, the cardiac murmur disappeared, and in two others murmurs appeared.

The average amount of Liquor arsenicalis given was 11·5 drachms (containing 0·276 grm. arsenic). This corresponds to only a little more than half the amount of arsenic which the patients in the neo-kharsivan group were receiving during approximately the same time. Two children presented signs of intolerance, one a neuritis and one a rash. Both cleared up speedily when the drug was discontinued. Seven patients had cardiac murmurs on admission, and only four on dismissal.

In the last group the salicylate of sodium was administered throughout the stay in hospital. None of the children showed any signs of intolerance. Eight patients had cardiac murmurs on admission, and nine on dismissal three months later.

In all, the results of the treatment of 45 cases are available for analysis, there being 15 cases in each group. Each group was further sub-divided as follows.

(*a*) Cases in which the chorea had been present less than thirty days before admission.

(*b*) Cases in which the chorea had been present from thirty to sixty days before admission.

(*c*) Cases in which the chorea had been present from sixty to ninety days before admission.

TABLE SHOWING RESULTS OF TREATMENT IN CHOREA.

	No. of cases.	Average duration in days of chorea previous to admission.	Average duration in days of chorea after admission.	Average total duration of chorea in days.
(A.) Cases treated with Neo-kharsivan.				
(*a*) 0—30 days ..	6	18	36	54
(*b*) 30—60 „ ..	5	41	62	103
(*c*) 60—90 „ ..	4	75	32	109
(B.) Cases treated with Liq. Arsenicalis.				
(*a*) 0—30 days ..	11	16	32	48
(*b*) 30—60 „ ..	4	45	28	73
(*c*) 60—90 „ ..	—	—	—	—
(C.) Cases treated with Sod. Salicylate.				
(*a*) 0—30 days ..	9	17	26	43
(*b*) 30—60 „ ..	6	37	30	67
(*c*) 60—90 „ ..	—	—	—	—

(*a*) Chorea present for less than 30 days before admission.
(*b*) „ „ „ 30—60 „ „ „
(*c*) „ „ „ 60—90 „ „ „

The results are summarized in the accompanying table. It is perhaps unfortunate that in some of the cases treated with neo-kharsivan (Group A), the chorea should have existed longer before coming under observation than was the case in the other two groups. However, even if one looks upon chorea as a self-limited disease, then the cases in Group A should have cleared up more quickly than those in the other groups, but this did not occur. Generally speaking, arsenic intravenously, although given in larger doses, seems to be less efficacious than liquor arsenicalis by mouth, and both of these measures less efficacious than sodium salicylate. Regarding the cardiac condition at the end of the stay in hospital, those in Group B (i.e., cases treated with arsenic by the mouth), show the best results.

In searching for a reason why cases treated with arsenic intravenously, although given relatively much larger amounts of arsenic, should take longer to clear up than those receiving liquor arsenicalis *per os*, one cannot avoid thinking that no matter how easily venipuncture is performed, a certain apprehension on the part of the patient is bound to exist, and it may well be that the slight additional emotional strain is responsible for the longer duration of the chorea. One must also remember that those patients receiving arsenic by the mouth three times daily are undoubtedly more constantly under the influence of the drug than are those who receive a massive dose intravenously

every fourth day. In any case, one is inclined to doubt the statement that the improvement in chorea is proportionate to the amount of arsenic given. The numbers under consideration are admittedly small, but in every sub-group except one (the 30 to 60 day period in Group A), the chorea disappeared in twenty-six to thirty-six days after admission to hospital. Generally speaking, the chorea disappeared in practically the same time after admission to hospital irrespective of drug treatment.

Although drug therapy would, then, appear to be of no value, the fact that chorea is a manifestation of the rheumatic infection suggests the advisability of giving salicylates. One does not infer, of course, that sodium salicylate is a specific for rheumatism, but of its value in some of the manifestations of rheumatism there can be no question, and because it may inhibit recurrences I consider its administration in chorea advisable.

Conclusions.

1. The course of chorea would not appear to be influenced by treatment with arsenic. The improvement, if any, probably results from its tonic action and is not in proportion to the amount of arsenic given. Intravenous arsenic has no advantages.

2. Rest in bed and freedom from emotional disturbances will usually cause a disappearance of chorea in four or five weeks.

3. The administration of sodium salicylate is recommended in the hope that it might have some good effect on the rheumatic infection.

REFERENCES.

1. Osler, W., *Prin. and Pract. of Med.*, Lond., 8th Ed., 1915, 1073.
2. Martin, T., quoted by Radcliffe, C. (see below).
3. Murray, W., *Rough Notes on Remedies*, 3rd Ed., 1899, 16.
4. Jacobi, A., *Therapeutics of Inf. and Childhood*, Philad. and Lond., 3rd Ed., 1903, 298.
5. Langmead, F., *Brit. Med. J.*, Lond., 1913, i, 1261.
6. Radcliffe, C., *Reynold's Syst. of Med.*, Lond., 1872, II, 212.
7. Bokay, J., *Deut. Med. Wchschr.*, Berlin, 1911, XXXVII, 111.
8. Bokay, J., *Ergeb. d. inn. Med. u. Kinderheilk*, Berlin, 1923, XXIV, 1.
9. Moffett, R., & Smith, C., *Arch. Ped.*, N.Y., 1924, XLI, 657.

ON THE ÆTIOLOGY OF HIRSCH-SPRUNG'S DISEASE.

BY

J. A. MUNRO CAMERON, M.B.,
Assistant Pathologist, Victoria Infirmary, Glasgow.

The signs and symptoms of congenital dilatation of the colon are well enough recognized to require no elaboration in this short communication, the purport of which is to describe a pathological basis for the disease and to report the results of the histological examination of two examples. I can find no reference to such histological changes as are recorded here in the relevant literature.

Both cases investigated were in boys, aged 10 and 7 years respectively, and were typical in every respect. The second case is described here.

Macroscopic Examination.

The colon is distended from the cæcum to the pelvi-rectal sphincter; its width being five times that of the sphincter. The wall above the sphincter is about four times the thickness of the wall at the sphincter, and the enlargement is chiefly confined to the circular muscular coat.

Microscopic Examination.

(*a*) *Through the distended area.* The mucosa, the muscularis mucosæ, and the submucous layers all show some fibrous thickening; the circular muscular fibres are greatly hypertrophied, the longitudinal to a lesser degree. The cells of Auerbach's plexus appear healthy but some fibrous change is apparent in their surroundings.

(*b*) *Through the sphincter.* No changes of importance are noted in the epithelial layer and glands, the muscularis mucosæ, or the submucous layer, although a few inflammatory cells are found throughout. The circular muscle coat is in sharp contrast to the area above and is of normal thickness, as also is the longitudinal layer, and shows little alteration apart from some fibrous and fatty degeneration. In the intermuscular plexus of nerve cells the changes are of a striking character. As the accompanying microphotographs (Figs. 1 and 2) show, the ganglia are replaced by inflammatory cells. In the ganglion which is shown under the higher magnification, only one nerve cell, shrunken and degenerated, is to be seen.

Fig. 1. Low power microphotograph through pelvi-rectal sphincter.

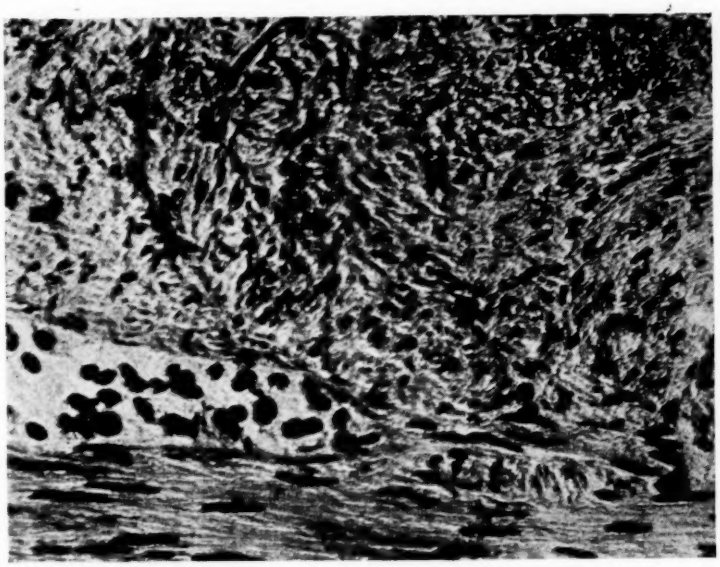

Fig. 2. High power microphotograph of ganglion in Auerbach's plexus.

A destructive lesion of the nerve ganglia at the pelvi-rectal sphincter will act as a direct obstacle to the descending peristaltic waves. Above it stasis of the contents will take place, and in an attempt to expel the accumulated and unaccustomed burden, the wall and especially the principal contracting part of it, the circular muscle layer, will hypertrophy.

The initial cause of the condition may be found in some inflammatory lesion of the rectum or anus, but as most of these cases are congenital, the probability is that meconium, retained in the relatively long and lax pelvic colon of the newly born, undergoes bacterial decomposition and sets up inflammatory changes in the mucosa. The inflammatory cells in their outward spread involve the ganglia, and an interruption of peristalsis results. Once a balance is struck between the distending bowel and the hypertrophy of its wall, a return to normal conditions is attempted, and at the sphincter the mucosa and muscular layers may recover from the inflammatory process, while the more highly organized layer of nervous tissue fails.

Hirschsprung's disease is therefore exactly comparable in its pathological basis to cardiospasm, as Hurst on clinical grounds has previously suggested. Although the lesion that I have recorded here is comparatively of old standing, it is so similar to the first cases of cardiospasm I described, that I have little doubt that if a sufficiently early case of megacolon is examined the results will be the same as in a case of acute cardiospasm published last year, in this journal[1], and the complete line of invasion by inflammatory cells will be found stretching from the epithelium to Auerbach's plexus.

It is not my province to deal with the surgical treatment of this condition, but so generally successful has dilatation of the cardia proved in cases of cardiospasm, that one naturally feels that similar dilatation of the pelvi-rectal sphincter might be given a reasonable trial.

REFERENCE.

1. Cameron, J. A. M., *Archiv. Dis. Child.*, Lond., 1927, II, 358.

HEART BLOCK ASSOCIATED WITH CONGENITAL HEART DISEASE.

BY

M. E. LAMPARD, M.B. (CANTAB).

The association of heart block with congenital heart disease has only been recorded in this century. Since then thirty cases have been published. It has usually been assumed that the block is due to a deficiency of the interventricular septum, but the majority of cases of this lesion show no block, and indeed there are cases where the septum is quite absent and yet the auriculoventricular node and bundle of His are present and acting smoothly. In this paper there is produced evidence to show that patency of the septum is not the sole cause of the heart trouble.

The case seen by the writer, reported by Firth in 1926, was that of a boy of six, complaining of frequent colds, and palpitation and shortness of breath of two years' standing. He lived in tenement buildings, and found difficulty in climbing the stairs to his flat. He had had diphtheria two years previously, but never rheumatic fever. His appetite was good and he was inclined to be constipated. He had never fainted. He went to a special school.

On examination, the sternum was seen to be depressed. There was no cyanosis. His lips were remarkably red, compared with his pale skin. There was no clubbing of the fingers. Pulsation was visible in the second and third intercostal spaces. The apex beat was in the fourth space, ¼in. beyond the nipple line. The pulse rate was 48. There was a pulmonary systolic thrill, and the shock of the closure of the pulmonary valves could be felt. The area of cardiac dullness extended up to the first intercostal space, two fingers' breadth to the left of the nipple line in the fourth space, and one finger's breadth to the right of the right border of the sternum. A harsh systolic bruit was audible in the pulmonary area. The aortic second sound was blurred and there was marked triple rhythm in the second and third left intercostal spaces.

This developed later into a blowing diastolic murmur replacing the pulmonary second sound, and audible all over the præcordia. The conus arteriosus beat visibly and very forcibly. Blood pressure was 116 mm. systolic and 64 mm. diastolic. X-rays showed the heart to be enlarged, globular, and rather high. The electrocardiogram showed complete heart block, the auricular rate being 75 and the ventricular 48. A later examination showed abolition of the T-wave in lead I; there was a question of a superimposed left ventricular lesion. Red blood cells numbered 4,320,000 per c.mm. and the hæmoglobin was 80%.

It is possible that the heart block was due to diphtheria, but a congenital origin seems more probable.

PREVIOUS CASES.

The first cases reported by previous authors were published by Morquio in 1901. Five members of one family had heart block of undoubted congenital origin, but there were no anatomical deformities of the heart. Two are given here.

CASE 2. (Morquio.) Male, aged 8 years. Full time. Frequent syncope, started by emotion, preceded by malaise and a sensation of emptiness.

CASE 3. (Morquio.) Male, 5 years. Also had attacks of faintness.

Both were apathetic and distrustful. Pulses irregular, unequal and very variable rate—50 to 70. No murmurs. Complete block. Autopsy on elder—heart dilated, otherwise normal macroscopically.

Case 4. (Scoseria.) Male, aged 4 years. Syncopes from 9 months. Pulse rate 40. Bulging of præcordia, systolic thrill and murmur at base. No cyanosis. ? Complete block.

Case 5. (V. Stark.) Male, aged 5 years. Pulse rate 28. Some syncopes. ? Complete block.

Case 6. (Van den Heuvel.) Female, aged 23 years. Syncopes since 2. Pulse rate 34. Some cyanosis. Loud basal systolic murmur. Complete block proved by polygraph. Atropine accelerated auricular rate only. Digitalis slowed it without affecting ventricles.

Case 7. (Fulton, Judson and Norris.) Male, aged 1 year, with constipation, pallor and sweating. Pulse rate 40 to 50. Heart a little enlarged to right. Systolic thrill and loud murmur. Pulmonary second sound accentuated. At 1¾ years, murmur only occasional. Heart enlarged, strong epigastric pulsation. Complete block shown by polygraph. Belladonna did not increase pulse rate. At 3 years, pulse rate 42, thrill and murmur had disappeared. Idea of patent interventricular septum finally abandoned. ? Cause of murmur. Father had a 3 to 1 heart block, and a sister a 2 to 1 block.

Case 8. (Zahorsky.) Female, aged 15 months. Growing very slowly. Restless and cyanotic; expiratory grunt. Poorly nourished. Pale and cyanotic. Pulse rate 54. Heart enlarged. Loud systolic murmur all over chest. Pulmonary second sound accentuated. Liver nearly down to umbilicus. Spleen not enlarged. Had a "seizure" at 12 months and another after eating popcorn. ? Stokes-Adams' attacks.

Case 9. (D'Espine and Cottin.) Male, aged 8½ years. Had had bronchitis and enlarged cervical glands. W. R. +; no other stigmata of syphilis. Feeble and puny. Pulse rate 20 to 32. Heart enlarged to left. Faint apical systolic murmur. No cyanosis nor clubbing. Red blood cells 5,301,500 per c.mm. Hb. 70%. 4 to 1 heart block by polygraph. Atropine did not affect the ventricular rate but slowed the auricles from 104 to 28, abolishing the block. This was not permanent. No explanation is forthcoming. Oculo-cardiac reflex slowed the ventricles from 28 to 24. Amyl nitrite—no change. The authors thought there was a congenital hole in the interventricular septum which was enlarged by a syphilitic process involving the bundle of His.

Case 10. (Whipham.) Female, aged 2 years. Full time, but backward. Well nourished, good colour, no clubbing. Pulse rate 48 to 80, full and regular. No cardiac symptoms. Heart enlarged to right. Outline globular under X-rays. Loud systolic murmur audible especially on left side from apex to base. 2 to 1 block and right-sided hypertrophy. P.R. interval long—·2 sec. (normal for age ·12 sec.). Red blood cells 8,400,000 per c.mm. and Hb. 110%.

Case 11. (Whipham). Female, aged 12 years. Measles at 6. Well grown, not cyanotic. Pain round heart on exertion, for 18 months. Pulse rate slow, 40 to 60, and slightly irregular. Occasionally a run of 3 to 5 beats at 80 to minute. Heart enlarged to left. Impulse heaving. Systolic murmur in 4th space. Rarely a diastolic whiff at apex and just outside it. Pulmonary second sound sometimes reduplicated. Electrocardiogram showed marked auriculo-ventricular dissociation and arrhythmia. Atropine increased pulse rate from 40 to 60. Red blood cells 4,800,000 per c.mm. Hb. 80%.

Case 12. (Bass.) Male, aged 15 years. Pneumonia at 3, measles at 5. Palpitations and dyspnœa. Poorly nourished. No cyanosis nor clubbing. Under normal height, weight and brain power. Pulse rate 40; 44 on exercise. Heart enlarged to left. Basal and apical systolic murmurs, former very loud and rough. Loud cervical venous hum. X-rays showed left side of heart enlarged. Complete heart block demonstrated by electrocardiogram. Wassermann and von Pirquet reactions negative.

Case 13. (Gorter.) Male, aged 6 months. Slight cyanosis. Pulse rate 72. Complete block. No syncopal attacks.

Case 14. (Josué.) Female, aged 18 years. Rheumatic fever at 18 months. Cyanosis on exertion and when moved emotionally; dyspnœa. Clubbed fingers. Heart considerably enlarged. Systolic thrill and murmur at base; thought to be pulmonary stenosis and patent interventricular septum. Electrocardiogram: P-R. interval ·22 sec. (normal ·12 to ·18) and Q-R-S. time ·14 sec., more than one-third of the whole complex (·38 sec.). In Lead I S-wave was very low and jagged and T-wave upright. In Lead III R-wave was very high and jagged

and T-wave was inverted and closer to S than normal. Josue thought that the left branch of the bundle of His was damaged, at the top of a patent interventricular septum, and that the lesion was congenital but might have been accentuated by the rheumatic fever.

CASE 15. (Rosenson.) Female, aged 10. Slight pain and distress over præcordia on considerable exertion. Full time; blue for several hours after birth. Had had pneumonia, diphtheria and whooping cough. No signs of heart trouble till age of 7 years. Apex beat in 5th space outside nipple line. Pulse rate 40 to 50. Heart enlarged to right and left. Long sawing systolic and diastolic murmurs, basal in origin. Electrocardiogram: complete block, auricular rate 100 and ventricular 48; left-sided preponderance. X-ray: right side of heart enlarged. No cyanosis and only slight dyspnœa after hopping 150 times. Thought to be a communication between the aorta and pulmonary artery just above the valves.

CASE 16. (Carter and Howland.) Female, aged 6 years. 6 lb. 9 oz. at birth. Had had a few syncopes, but no dyspnœa even on exertion. No cyanosis. Apex beat in 5th space 3¼in. from mid-line. Pulse rate 37. Heart slightly enlarged. Harsh rough systolic murmur loudest at apex but not conducted. Complete block by electrocardiogram. At the age of 10 the murmur was only just audible.

CASE 17. (Smith.) Male, aged 20 years. Syncopes from 3 till 9 years, but could now play games and dance, and was robust and moderately muscular and well developed. Apex beat circumscribed, distinct and striking. Pulse rate 43. Heart enlarged to the left. Apical and basal systolic murmurs. Electrocardiograms showed complete heart block except in forced expiration when there was none. Under X-rays the heart was seen to be higher and more horizontal in forced expiration, therefore there was less tension on the heart, and this tension on the interventricular septum was thought to be the "last straw" to complete the heart block. Atropine did not affect the rhythm of the ventricles. Wassermann reaction negative. Red blood cells, 5,120,000 per c.mm., Hb. 98%. white cells 9,100 per c.mm.

CASE 18. (White, Eustis and Kerr.) Female, aged 4 days. A seventh child; full time; parents, brothers and sisters all well. Irregularity of heart noted before birth. Pulse rate varied rapidly between 80 and 160, at both of which rates it was regular; but at times there was bigeminy at 105 or trigeminy at 120. Cyanosis at first, not later. Electrocardiogram showed a variable block of 2 or 3 to 1 and less: right-sided preponderance. No murmur. At 5 weeks the child was seen to be a Mongolian idiot. No clubbing; cyanosis again. Blowing basal systolic murmur. No block; pulse rate 160. At eleven weeks the child was under nourished and apathetic. No cyanosis and no clubbing. Heart very large and globular. At 5 months she weighed 10 lbs.; the pulse rate ranged from 70 to 140. The condition of the block was sometimes 2 : 1, sometimes 4 : 3 and sometimes the block was absent. At 8 months a faint diastolic murmur was heard at the base. The pulse was regular at 110 and there was no block; the P-R. interval was ·1 sec. (normal for her age). The authors thought the ductus arteriosus was patent.

CASE 19. (Same authors.) Male, aged 6. Full time. Wassermann reactions of parents positive, but boy appeared healthy. Broncho-pneumonia at 6 years. He had failed to gain in weight since tonsillectomy at 5. Very nervous and weak. Dyspnœa and cyanosis on exertion, but no clubbing. There was visible contraction over the præcordia and a marked carotid pulse. The apex beat in 6th space was in the nipple line and there was systolic retraction. The beat was slow, forceful and heaving in the epigastric angle. No thrill. Pulse rate 46 when he was erect, 60 after exercise. Heart enlarged to right and left. Loud apical systolic murmur after exercise only, not well conducted. The pulmonary second sound was reduplicated. B.P., 90 mm. systolic, 65 diastolic. The liver and spleen were not palpable, but the superficial lymph glands were enlarged and hard. The von Pirquet test was negative, but the Wassermann reaction was strongly positive. X-rays showed a large round heart, central in position. Complete block was shown by electrocardiogram, auricular rate being 120 and ventricular 45. Thus the condition is only probably of congenital origin, as a gumma may have destroyed part of the bundle of His or the A-V. node.

CASE 20. (Willius.) Male, aged 20. Cyanotic and fretful in first 2 years. Influenza at 17. Had a troublesome cough. Was pale in childhood and developed slowly. Pulse rate 63. Heart enlarged on both sides. Many extra systoles and a systolic thrill. A loud rough reverberant systolic murmur was audible all over the præcordia, up the neck, especially on the left

side, and out to the left shoulder. B.P., 112 mm. systolic, 82 diastolic. X-rays showed dilatation of right ventricle. The lesion was thought to be pulmonary stenosis and a patent ductus Botalli. In Lead II of the electrocardiogram the P-wave was inverted, because of a change in the position of the pacemaker node. This doubtless accounts for the extra systoles. The T-wave in Lead II was very exaggerated and peaked. Heart block complete, auricular rate 57, ventricular 63. This is very remarkable and presumably due to the failure of the sino-auricular node. The fingers were clubbed. The liver was not felt. Red blood cells, 7,400,000 per c.mm.; Hb. 95%; white cells 9,200 per c.mm.

Case 21. (Barbier, Lebée and Mouquin.) Male, aged 15. Complained of dyspnœa on exertion for 3 weeks: had never fainted and was not cyanotic. The apex beat was in the nipple line in 6th space. Pulse rate was 30. Heart enlarged to right. Loud harsh basal systolic murmur conducted to left. X-rays showed the heart to be globular and enlarged. Complete block by electrocardiogram. When the eyes were compressed the pulse rate slowed down to 20 and the boy fainted. He was thought to have a patent interventricular septum.

Case 22. (Meyer.) Female, aged 18. Seventh child; others all healthy. Lips, hands and feet were blue and congested in infancy. Fingers clubbed early. She could not play or run at school because of dyspnœa. The legs had never swollen. She complained of palpitation in right side of chest. Feeble and poorly developed but intelligence normal. Very cyanotic. She had a parenchymatous goitre. Apex beat in 4th space in right nipple line. Pulse rate varied between 63 and 80, and was regular but for extra systoles. Systolic thrill. Heart enlarged to left. Sharp first sound, and an intense harsh systolic murmur audible best over the sternum, and conducted up the carotid arteries. Second sounds feeble. X-rays showed the heart on the right. The aorta, stomach and liver were also found to be transposed. The electrocardiogram showed right-sided preponderance. Atropine did not affect the ventricular rate but ocular compression had a very peculiar effect, as follows:—

	Auricular rate.	*Ventricular rate.*
Normal	100 ..	66
Weak compression	112 ..	80
Strong compression	55 ..	80

Thus weak compression increased the rate of all the chambers, but the auricles were greatly slowed and the ventricles unaffected by strong compression. Red blood cells 6,700,000 per c.mm. and Hb. 130%. White cells 11,000 per c.mm. W.R. negative.

Case 23. (Gibson.) Female, aged 12. Complained of loss of weight and appetite. Usually enjoyed good health but was not as active as her playmates. Suggestion of cyanosis. Pulse slow and regular—rate 50. Heart slightly enlarged to left. Basal systolic murmur to left of sternum. Complete block by electrocardiogram. Regarded as probably a patent interventricular septum.

Case 24. (Romberg and White.) Female, aged 9 months. Brought up for constant crying and excessive perspiration. Full time. The midwife thought she would die at birth. Cyanotic then; now only when she cries. Fairly well developed and nourished. Pulse rate 60 to 70; frequent arrhythmia. No thrill. Heart not enlarged to percussion. Loud systolic murmur in lower præcordia. Suspicion of a diastolic bruit at apex and towards sternum. Complete block shown by electrocardiogram; auricular rate 160, ventricular 70. No œdema nor clubbing. Liver and spleen not felt. A month later a long diastolic murmur was heard. Diagnosis:—probably a patent interventricular septum and possibly a patent ductus arteriosus.

Case 25. (Leconte.) Female, aged 3. Diphtheria and whooping cough at one year. Broncho-pneumonia at 2, when her pulse rate had never exceeded 80. No dyspnœa, cyanosis nor fits. Child was pale but normally developed. Pulse rate 48. Systolic murmur loudest in pulmonary area. Diastolic murmur and reduplication of pulmonary second sound. Complete block and right-sided preponderance shown by electrocardiogram. Leconte diagnosed mitral stenosis and patent interventricular septum, and congenital rupture of the bundle of His. He wondered whether the hole in the septum had been enlarged during the diphtheria.

Case 26. (Wilson & Grant.) Female, aged 14 months. Persistent vomiting. Frail and blue from birth. Bronchitis frequently. One sister with congenital dislocation of the hip. Weight 12½ lbs. No signs of syphilis. General cyanosis, particularly of the cheeks, lips, fingers

and toes. Distended venules in cheeks and limbs. Nose bulbous and fingers and toes clubbed. Pulse rate 66. Heart enlarged on both sides to percussion, and seen to be very big and globular when screened. Rough systolic murmur and thrill especially at base. Liver enlarged, its edge being in right iliac fossa. Slight œdema of the legs. Scattered rhonchi over both lungs but no signs of effusion or consolidation. Red blood cells, 1,111,000 per c.mm., and Hb. 128% ; white cells 27,800 per c.mm. (If these figures are correct, each red cell contained more than 5 times its normal amount of hæmoglobin.) Wassermann reaction of blood negative. Electrocardiogram : two to one heart block. P-wave upright in all leads and very large in lead II. Ventricular complexes normal, Q-wave being present in leads II and III. The extra auricular waves were superimposed on the preceding T-wave. Diagnosis : congenital pulmonary stenosis and patent interventricular septum. For a fortnight the child improved ; the vomiting ceased, the œdema and liver enlargement disappeared, and the weight increased. Pulse rate usually varied between 60 and 70, and never exceeded 100. Thereafter the vomiting returned, with diarrhœa ; the signs of heart failure again appeared, with intense cyanosis, and the child died suddenly.

At autopsy all the organs were found to be congested. The kidneys were fused on the right side, but with separate pelves and ureters. There was hydronephosis of the left element, with constriction of the pelvi-ureteral junction. The heart weighed 2 oz., and was globular. The aorta was very wide and flattened antero-posteriorly. It gradually narrowed as it descended. The pulmonary artery was much reduced in calibre and indeed was quite cut off from the ventricular cavity. At its junction with the ductus arteriosus, which had an external diameter of 3 mm., it measured 5 mm. across. The right auricle was large, and the venæ cavæ dilated, but the left auricle was very small. The ventricle was a common one, with no definite septum. Its wall was thick, and fibrous in the right upper portion. A large aortic orifice was placed centrally. The tricuspid valve was deformed but not stenosed. The mitral valve was normal. A rounded muscular prominence running down the posterior wall alone represented the septum. The endocardium over it was thickened and below the former lay the left branch of the bundle of His. The A-V. node was well developed, but the conducting fibres coming from it were interrupted and broken up by the fibrous tissue of the central fibrous body, only to re-unite and divide normally into right and left branches lower down. None of the fibrous tissue seemed inflammatory in origin.

Note.—It is remarkable that there was a normal Q-wave in the electrocardiogram, for this wave is supposed to represent the spread of the impulse of contraction through the septum, which in this case was absent. Possibly a large mass of muscle in the area of the conus arteriosus, when stimulated in an upward direction, might have given rise to the Q-wave, but it was not related specially to the conduction system to allow of its early excitation. Doubtless the fibrous tissue which broke up the A-V. node produced the partial heart block.

Case 27. (McIntosh.) Female, aged 7 months. Good family history. Full time. Pneumonia at 3 months. Much indigestion after weaning. She had a persistent cough and slept badly. At 7 months she weighed only 7½ lbs. and was poorly developed, under-nourished, weak and fretful ; pale but not cyanotic. The cervical, inguinal and axillary glands were enlarged. Pulse rate 57 to 64. No thrill. Heart a little enlarged to left. Prolonged systolic murmur, loudest at apex. Complete block shown by electrocardiogram ; auricular rate 136, ventricular 57 ; right-sided preponderance. T-wave upright in all leads. Liver 2 cm. below costal margin ; spleen just felt. No clubbing. Red blood cells, 3,600,000 per c.mm. ; white cells 12,850 ; Hb. 60%. Wassermann reaction and von Pirquet negative. She died a month after admission to hospital, but there was no autopsy.

Case 28. (Aldrich.) Female, age not given. She played games actively and was fond of swimming. No dyspnœa and very slight cyanosis. Pulse rate 45. Congenital heart disease ; a 3 to 1 block proved by electrocardiogram. One day she dropped down dead in the water before her swim. No autopsy.

Case 29. (Davis.) Age and sex not given. Child did not gain weight normally. Neither cyanosis nor clubbing. Author thought there was a patent interventricular septum. Complete heart block shown by electrocardiogram ; auricular rate 125, ventricular 45. Atropine did not accelerate the pulse rate.

CASE 30. (Shapiro.) Female, aged 9. A typical blue baby from birth. Always below weight and under-nourished. Tired easily and became very blue when she played games, as she did habitually. Persistent dry cough and insomnia. Whooping cough at 6 months, measles at 2 years, influenza at 3, and pneumonia at 4. Deep cyanosis of face and all mucuous membranes. Fingers and toes clubbed. Eyes prominent and sclerotics blue. Marked pulsation of veins of neck, which was double the rate of the radial artery, 88 to 44. Bulging of the præcordia. Basal systolic thrill. Heart considerably enlarged, especially to left. Sounds slow, regular and of good quality. Prolonged harsh systolic murmur, loudest in pulmonary area. Moist râles at bases of both lungs. Liver and spleen not felt. No œdema. Tonsils and cervical lymph glands enlarged, and copious thick discharge from left ear. Provisional diagnosis: Pulmonary stenosis. By X-rays heart was seen to be enlarged to right and left. Electrocardiogram: auricular rate 130, ventricular 65. P-R. interval ·28 sec. (normal ·18 sec.). In lead I, P-wave was exaggerated and T-wave inverted. P-wave highest in lead II, where it was almost as high as R-wave: right-sided proponderance, and 2 to 1 block.

CASE 31. (Nissé.) Male, aged 7 years. Had had measles and whooping cough; bronchitis every winter. Broncho-pneumonia when nearly 2. Complained of occasional palpitation at night. No syncope. Well developed, and bright mentally. No cyanosis and no clubbing. Pulse rate regular at 48. Heart a little enlarged on both sides. No thrills. Harsh systolic murmur heard all over præcordia, especially in pulmonary area. B.P. 90 mm. systolic, 60 mm. diastolic. Electrocardiogram: complete block at one time (auricular rate 92, ventricular 45); 2 to 1 block at another time.

DISCUSSION.

An Analysis of these Cases (see Table) shows them to be fairly equally divided as to sex, there being 14 cases of boys and 16 girls. All became evident in childhood, but at different periods. It is striking that many were not diagnosed for a considerable number of years. Indeed the average age for the slow pulse to be first noted is $6\frac{3}{4}$ years. Nor were the fainting attacks, if present, found in the earliest years. Cardiac enlargement was, of course, fairly constant. Naturally the most frequent lesion was patent interventricular septum, but it is remarkable that in the only case where an autopsy is recorded, although there was no septum, yet the block was not due to its absence, but to fibrous tissue in the A-V bundle. This is hinted at in another case when heart block is complete except during complete expiration, when the position of the heart is at its highest, and consequently tension on it at its lowest. For it is not partial interruption of the bundle, but pressure thereon, that produces heart block. Some of the hearts were low in position, reaching to the 6th space, and therefore stretched.

The slowest pulse rate recorded varied from 20 to 72, and averaged 47. Had the observations been taken on adults, the average would have been lower. Cyanosis was observed less frequently than one would expect, seeing that not only the circulation, but also the cardiac rhythm, was disturbed.

There were 23 cases of complete heart block, and 3 cases of a 2 to 1 partial block. One case showed a 3 to 1 block; one varied between a complete and a 2 to 1 block; one case had a block which at times was partial (2 to 1 and 3 to 1) and at other times less. Another had complete block except at full expiration, when there was none. One showed delayed conduction, with a lesion in the left branch of the bundle of His.

Author.	Sex	Age of proof of lesion.	Age when slow pulse observed.	Congenital Malformation.	Cardiac enlargement.	Grade of block.	Slowest pulse rate.	Cyanosis.	Syncope.	Year.
Writer's case ..	M	6 yrs.	5 yrs.	? Patent interventricular septum	+	C	48	0	0	1928
Morquio ..	M	8 ,,	4 ,,	None	0	? C	50	0	++	1901
	M	5 ,,	3 ,,	None	+	? C	50	0	++	
Scoseria	M	4 ,,	4 ,,	?	+	? C	40	0	+	
Von Stark ..	M	5 ,,	4 ,,	?	?	? C	28	?	+	1903
Van den Heuvel	F	23 ,,	15 ,,	Patent interventricular septum	?	C	34	(+)	+	1908
Fulton, Judson & Norris	M	1¾ ,,	1 ,,	Patent interventricular septum	(+)	C	40	0	0	1910
Zahorsky ..	F	15 mths.	1 mth.	? Patent interventricular septum	+	C	54	+	2	1915
D'Espide & Cottin	M	8 yrs.	8 yrs.	?	(+)	C	20	0	0	1915
Whipham ..	F	2 ,,	2 ,,	Patent interventricular septum	+	2 : 1	48	0	0	
	F	12 ,,	6 ,,	Patent interventricular septum	+	C	40	0	0	1915
Bass	M	15 ,,	13 ,,	?	+	C	40	0	0	1918
Gorter	M	6 mths.	6 mths.	?	?	C	72	(+)	0	1919
Josué	F	18 yrs.	18 yrs.	Pulmonary Stenosis and patent interventricular septum	++	delayed conduction	?	++	0	1919
Rosenson ..	F	10 ,,	7 ,,	Opening from aorta to pulmonary artery ..	++	C	40	0	0	1920
Carter & Howland	F	6 ,,	6 ,,	Patent interventricular septum	(+)	C	37	0	(+)	1920
Smith	M	20 ,,	20 ,,	?	(+)	C & O	43	0	early +	1920
White, Eustis, & Kerr ..	F	4 days	before birth	Patent ductus arteriosus	++	2·1 & less	70	(+)	0	
	M	6 yrs.	5½ yrs.	?	+	C	45	(+)	0	1921
Willius	M	20 ,,	20 ,,	Pulmonary stenosis and patent ductus Botalli	+	C	63	early	0	1921
Barbier, Lebée & Mouquin ..	M	15 ,,	15 ,,	Patent interventricular septum	+	C	30	0	0	1922
Meyer	F	18 ,,	?	Pulmonary stenosis and patent interventricular septum	++	C	63	++	0	1923
Gibson	F	12 ,,	12 ,,	? Patent interventricular septum	(+)	C	50	trace	0	1923
Romberg & White	F	9 mths.	9 mths.	Patent interventricular septum	0	C	60	(+)	0	1924
Leconte	F	3 yrs.	2 yrs.	Patent interventricular septum and mitral stenosis	?	C	48	0	0	1924
Wilson & Grant ..	F	14 mths.	14 mths.	No interventricular septum	+	2 : 1	66	++	0	1926
McIntosh ..	F	7 ,,	7 ,,	?	(+)	C	57	0	0	1926
Aldrich	F	?	?	?	?	3 : 1	45	(+)	0	1927
Davis	?	?	?	Patent Interventricular septum	?	C	45	0	0	1927
Shapiro	F	9 yrs.	8 yrs.	? Pulmonary stenosis ..	++	2 : 1	44	++	0	1927
Nissé	M	7 ,,	7 ,,	?	+	C & 2 :1	45	0	0	1928

The effect of atropine, mentioned in seven of the cases, was to accelerate the ventricles in one; in the others the rate was unchanged. In one case the auricles were retarded.

Where a blood count was reported, there was usually a polycythæmia (5 cases out of 8) but the hæmoglobin was 100 per cent. in one case, increased in 3, and decreased in 5.

The prognosis is naturally of great importance. One case died on entering the water to swim, though he had previously swum frequently. Others had relatively sudden heart failures and died in a few days or weeks. But it is remarkable that some infants lost their heart block, while the lesion in other children was not noticed until they were in their teens, and some even played games and led an ordinary life. Doubtless in every case where the heart block and cardiac murmurs and enlargement persist great caution should be enjoined, and no games or violent exertion permitted. But from the point of view of the child, when there are no symptoms, an ordinary life, even though a slightly dangerous one, seems preferable to an existence hedged about with restrictions. Every case, however, nust be judged on its own merits, and considerations such as the size of the heart, the ventricular rate, the degree of heart block, and the response to exercise, be weighed and judgement delivered accordingly.

Conclusions.

1. In certain rare instances of congenital heart disease there may be heart block of congenital origin.
2. This heart block is usually associated with an anomaly of the inter-ventricular septum.
3. It is probably due, not so much a hole in the septum, as to the presence of fibrous tissue causing pressure on the bundle of His.
4. Where there is a hole in the septum, the bundle may run on the edge thereof, and be liable to damage by inflammation, causing partial destruction of the septum, in rheumatic fever, syphilis and possibly diphtheria.
5. Where patients with this disease lead comparatively normal lives they are liable to sudden death.

REFERENCES.

Aldrich, C. A., *Amer. J. Dis. Child.*, Chic., 1927, XXXIV, 1090.
Barbier, Lebée & Mouquin, *Bull. Soc. Péd. de Paris*, Paris, 1922, XX, 11.
Bass, M. H., *J. Am. Med. Ass.*, Chic., 1920, LXX, 287.
Carter, E. P. & Howland, J., *Bull. Johns Hopkins Hosp.*, Balt., 1920, XXXI, 351.
Davis, J. H., *Am. J. Dis. Child.*, Chic., 1927, XXXIV, 133.
D'Espine, A. & Mlle. Cottin, *Bull. Acad. de méd.*, Paris, 1915, LXXIV, 292.
Firth, D., *Proc. R. Soc. Med.*, Lond., 1925-6, XIX (Clin. Sect.), 26.
Fulton, Z. M. K., Judson, C. F. & Norris, G. W., *Amer. J. Med. Sc.*, Philad., 1910, CXL, 339.
Gibson, S., *Am. J. Dis. Child.*, Chic., 1926, XXXIV, 1090.
Gorter, E. M., *Nederl. Maandschr. v. Gen.*, Leiden, 1919, V.
Josué, M. O., *Bull. et mém. Soc. méd. d. hôp. de Paris*, Paris, 1919, XLIII, S.3, 408.
Leconte, *Ibid*, 1924, XLVIII, S.3, 488.
McIntosh, R., *Am. J. Dis. Child.*, Chic., 1927, XXXIV, 965.
Meyer, P., *Arch. d. mal du coeur*, Paris, 1923, XVI, 16.
Morquio, *Arch. de méd. d. enf.*, Paris, 1901, IV, 467.

Nissé, B. S., *Proc. R. Soc. Med.*, Lond., 1927-8, XXI (Clin. Sect.), 438.
Romberg, E. C. & White, P. D., *Bost. Med. & Surg. J.*, Boston, 1924, CXC, 591.
Rosenson, W., *Arch. Ped.*, N.Y., 1920, XXXVII, 103.
Scoseria, *Arch. de méd. d. enf.*, Paris, 1901, IV, 467.
Shapiro, M. J., *Minnesota Med.*, St. Paul, 1927, X, 566.
Smith, S. C., *J. Am. Med. Ass.*, Chic., 1921, LXXVI, 17.
Van de Heuvel, G. C. T., *Proefschr. aan Ryks Univers.*, Groningen, 1908.
Van Stark, W., *Monatsschr. f. Kind.*, Leipsig, 1903, II, 11.
Whipham, T. R., *Brit. J. Child. Dis.*, Lond., 1915, XII, 321.
White, P. D., Eustis, R. S. & Kerr, W. J., *Am. J. Dis. Child*, Chic., 1921, XXII, 299.
Willius, F. A., *Bost. Med. & Surg. J.*, Boston, 1921, CLXXXIV, 64.
Wilson, J. G. & Grant, R. T., *Heart*, Lond., 1925-6, XII, 295.
Zahorsky, J., *Interstate Med. J.*, 1915, XXII, 57.

HEART BLOCK ASSOCIATED WITH CONGENITAL MALFORMATION OF THE HEART.

BY

G. B. FLEMING, M.D., F.R.F.P.S., AND MARY M. STEVENSON, M.A., M.D.
(From the Medical Department, Royal Hospital for Sick Children, Glasgow.)

Heart Block in congenital malformation of the heart is comparatively rare. The following two cases came under observation in the Royal Hospital for Sick Children, Glasgow.

CASE 1. D. H., male, aet. 3½ years. The labour was normal and the child was full term and healthy at birth. Except for a mild attack of measles when 1½ years old and a burn at the age of a year and nine months, he was quite healthy and throve well until 3 months before admission to hospital when he had a "bad turn" lasting all night. During this he became pale and unconscious and his mother thought his "heart had stopped." Since then he has appeared very tired at night and his appetite has been poor.

On admission to hospital he was found to be a fair-sized moderately nourished boy. He did not appear ill. His height was 91·5 c.mm., and he weighed 11·89 kg. The skin was clear. There was no clubbing of the fingers nor cyanosis. Examination of the lungs, abdomen, nervous system and urine was negative. The tonsils were enlarged and the teeth carious.

The heart was enlarged, the apex beat being in the 5th space 3 inches from the middle line, the left border of cardiac dullness 3½ inches from the midline, the right border 1 inch to the right of the midline and the upper border at the level of the third rib. Radiograms showed increased heart shadow both to the right and to the left. The cardiac pulsations were forcible. A loud systolic murmur was heard all over the præcordia. This was best heard midway between the apex and the midline; it was fairly well conducted to the axilla but was also conducted towards the right shoulder. The second sound was double both at the apex and the base. The heart rate was 46 per minute. The von Pirquet, Wassermann and the Schick tests were negative. The blood culture was sterile. The hæmoglobin was 78 per cent. (Haldane) and the red cells numbered 4,200,000 per c.mm. On making a fluoroscopic examination of the heart the auricles could be seen beating at an independent and more rapid rate than the ventricles.

The boy remained under observation in hospital for four months and during this time his pulse rate varied between 30 and 60 per minute, only occasionally rising to slightly over 50, but never falling below 30 per minute. Even when the child was up and going about, it rarely exceeded 50 per minute. During his stay in hospital the boy's general condition improved greatly but the condition of the heart remained unchanged. There were no syncopal nor cyanotic attacks.

CASE 2. Female, aet. 8 years. The child was very small at birth, weighing only 4 lb., but seemed healthy. She was always small and delicate; she did not walk till three years of age and did not talk till five. When one year old it was noticed that the hands, feet, lips and cheeks were blue and that the fingers were becoming clubbed. Ever since she began to walk she has had frequent fainting attacks. She has never been able to walk quickly and has always been easily tired.

On admission to hospital she was found to be a spare child weighing 22·7 kg. The hands, feet, lips and cheeks were definitely cyanosed and the fingers and toes were clubbed. There was rhinitis. The lungs were clear. The liver could be felt two finger-breadths below the costal margin. The heart was enlarged. The apex beat was in the 5th space, 2¾ inches from the midline, the left border of cardiac dulness was 3½ inches to the left and the right border ¾-inch to the right of the midline, the upper border on a level with the third rib. A loud systolic murmur could be heard all over the præcordia with its maximum intensity at the third left costal cartilage and was well conducted to the left clavicle. Behind, the murmur was well heard in the left inter-scapular region at the level of the 4th vertebra and was well conducted towards the left scapula. There was slight fever on admission and the pulse rate at first was between 80 and

90 per minute. On the third day in hospital the pulse rate fell to 60 and thereafter, until dismissal, remained between 45 and 65 with occasional rises to 85 per minute. Throughout her stay in hospital there were no syncopal attacks and the cardiac condition remained unchanged. There were 6,100,000 red cells per c.mm. and the hæmoglobin was 99 per cent. The von Pirquet and Wassermann reactions were negative. The child was backward mentally, her mental ratio being 53 (Binet Simon).

The patient was discharged from the hospital in August, 1922, and subsequently came under the care of Dr. Cowan at the Glasgow Royal Infirmary to whom and Dr. Rennie we are indebted for the electrocardiographic records. She was under observation there, at intervals, for several years without there being any notable change in the condition. Subsequently she died at home. There was no post-mortem examination.

In Case 1 it is possible that the cardiac lesion was acquired during some acute infection, e.g., unrecognized diphtheria. We know, however, that the bradycardia had been present when the child was twenty-one months old, for he then suffered from burns and was admitted to the Victoria Infirmary, Glasgow. On admission there his pulse rate was 72 per minute, but within three days it fell to 48 per minute and remained about 50 per minute during the remainder of his stay in that hospital. This, in conjunction with the evidence of congenital malformation of the heart afforded by physical examination, makes it practically certain that the bradycardia is of congenital origin.

From the history of Case 2 it is certain that the cardiac lesion had existed since infancy, but unfortunately we have no early records of the pulse rate.

Electrocardiographic Records.

Case 1. Complete and permanent a-v block was present (Fig. 1). The auricular rate varied from about 80 per minute to 125 per minute, and the ventricular from about 35 to 50 per minute. The rhythm of the ventricles was almost regular and that of the auricles slightly irregular. On one occasion an auricular beat failed for no apparent cause (Fig. 2), and on another occasion ventricular beat was missed; this was after exertion (Fig. 3).

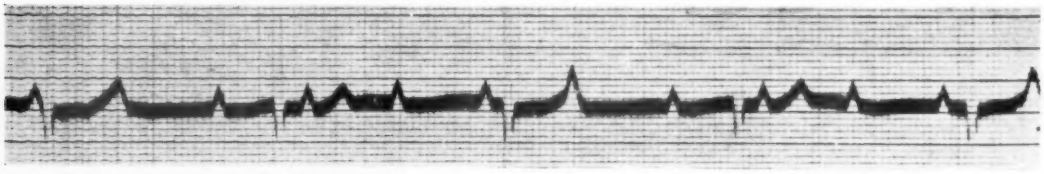

Fig. 1. Case I. 3 Complete dissociation of auricular and ventricular contractions

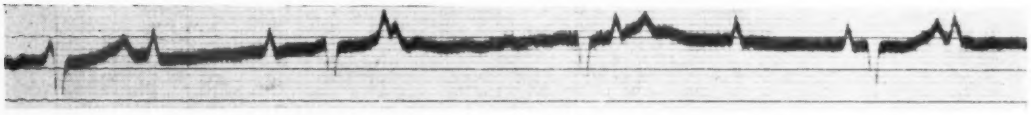

Fig. 2. Case I. Asystole of the auricles

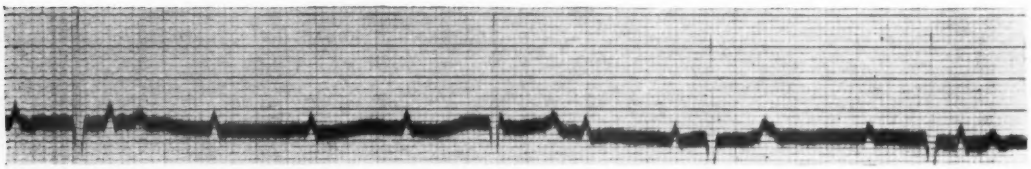

Fig. 3. Case I. Asystole of the ventricles

The P deflections are large and seem quite normal, as also do the Q.R.S. deflections except where they are interfered with by one of the P deflections. The Q-T interval is prolonged measuring slightly over 0·4 second. The T deflection is positive in leads I and II, but sometimes inverted in lead III.

The effects of exertion and the injection of atropine and of adrenalin were studied. The block was quite unaltered by any of these procedures. Tables I, II and III give the rates of the auricles and ventricles immediately before and after each.

TABLE I.

THE EFFECT OF EXERTION.

	Before.	½ min. after.	1 min. after.	2 mins. after.	3 mins. after.
Auricle	89	—	97	95	98
Ventricle	37	—	39	?*	39
Auricle	98	123	100	103	—
Ventricle	39	41	40	40	—

*Asystole of the ventricle.

TABLE II.

THE EFFECT OF ATROPINE GR. 1/200.

	Before.	9 mins. after.	19 mins. after.	26 mins. after.	40 mins. after.	45 mins. after.
Auricles..	86	93	86	98	104	107
Ventricles	36	44	36	43	38	49

TABLE III.

THE EFFECT OF ADRENALIN 0·5 CC. 1 IN 1,000.

	Before.	2 mins. after.	5 mins. after.	10 mins. after.	13 mins. after.
Auricles	116	115	115	107	107
Ventricles	45	47	47	47	47

The exertion consisted in the patient raising himself rapidly to a sitting position in bed and lying down again 20 times; this was sufficient to make him slightly out of breath. It will be noted that the auricular rate was slightly increased but that there was practically no alteration in the ventricular rate.

After the injection of 1/200 gr. of atropine there was a definite increase in the rate of both the auricles and the ventricles. Half an hour after the injection of the drug the patient showed definite signs of its action, flushed dry skin and dilated pupils, but the block persisted. ½ c.cm. of adrenalin (1 in 1,000) injected subcutaneously had practically no influence on the ventricular rate, but there was slight slowing of the auricular rate. These tests exclude the possibility that the block was of nervous origin. Pressure on the vagus in the neck was tried on two occasions. This had no effect on the rate or rhythm of the radial pulse.

The results of these tests show almost certainly that there was a complete hiatus in the conducting fibres somewhere between the auricles and the ventricles, the probability being that there was absence of that part of the inter-ventricular septum through which the a-v bundle passes.

CASE 2. The curves show 2-1 block, the auricular rate being twice that of the ventricular, every second auricular beat being blocked (Fig. 4). The Q deflection is present and the R.T. interval is not unduly prolonged. The T deflection is positive in all leads. Very similar curves were obtained in Wilson and Grant's[1] case,

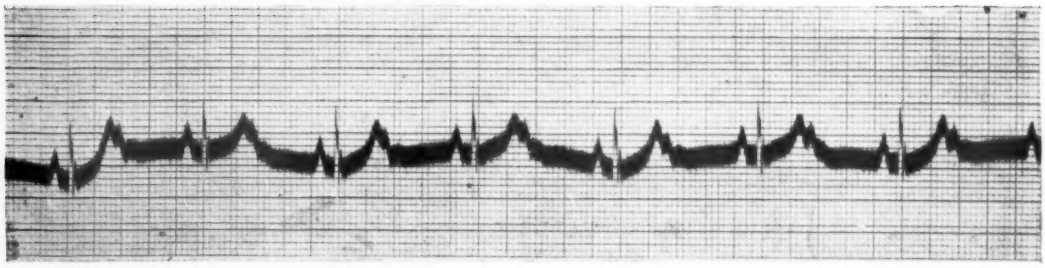

FIG. 4. Case II. 2–1 Heart Block. The blocked auricular contractions immediately follow the T waves

The effect of exertion and the injection of atropine are shown in Tables IV and V. After the pulse rate had been increased by exertion and the giving of atropine the T wave became single (Fig. 5). It seems clear that the blocked P wave became completely fused with T. This seems the most reasonable explanation of the disappearance of the blocked P wave for it is extremely unlikely that the action of either atropine or exertion would be to slow the auricular rate. This view is confirmed by tracings taken on one occasion immediately after exertion where there was irregularity (Fig. 6). In this curve each physiological beat is followed by a ventricular extra systole and in the long pause following this a blocked auricular complex can be clearly seen.

TABLE IV.

PULSE RATE.

Before exertion	49	
Immediately after exertion	68	irregular.
1 minute after exertion	68	,,
2 ,, ,, ,,	68	,,
3 ,, ,, ,,	50	,,
4 ,, ,, ,,	50	,,

TABLE V.

PULSE RATE.

Before atropine gr. 1/60	52
1½ minutes after	56
5½ ,, ,,	52
9 ,, ,,	52
13 ,, ,,	64
14 ,, ,,	66
19 ,, ,,	78

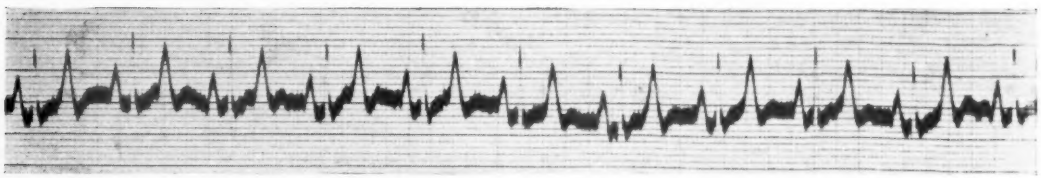

FIG. 5. Case II. After atropine the blocked P waves fuse with T

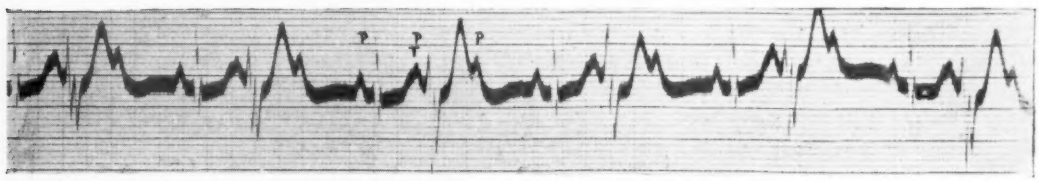

FIG. 6. Case II. After exertion the heart's action becomes irregular. A normal beat is followed by an extra systole and in the long pause succeeding this a blocked P wave can be seen

Discussion.

The cardiac deformity most likely to produce heart block is absence of, or defect in, the upper part of the inter-ventricular septum and although this is the most common cardiac deformity (Abbott[2]) congenital heart block seems to be rare. Probably the fact that the usual site of the septal defect is anterior to the pars membranacea whilst the a-v bundle lies behind it, explains the comparative rarity of the condition. In the only case in which a post mortem examination of the junctional tissues has been made (Wilson and Grant's[1] case) there was a gross defect in the ventricular septum and the fibres of the bundle were found to be seriously affected, though there was still a tenuous connection of primitive tissue between the auricles and the ventricles. In this case there was partial (2-1) block. There is a striking resemblance between this and our second case. In both there was cyanosis and clubbing of the fingers, in both the cardiac signs pointed to pulmonary stenosis, and in both the electrocardiogram showed 2-1 block, the T-wave being split by the blocked P-wave.

We have been able to trace in the literature records of nineteen authenticated cases. The first twelve of these have been summarized by White, Eustis and Kerr[3]. Since then cases have been reported by Rhomberg and White[4] (one case), Frias[5] (one case), Barbier, Lebée and Mouquin[6] (one case), Wilson and Grant[1] (one case), Lukin and Frey[7] (one case), McIntosh[8] (one case) and Nessé[9] (one case), while recently Schlesinger[10] has reported a case in which there was branch bundle block. The majority showed complete a-v block (16 cases) while in three the block was partial. In the cases where the block was complete the pulse rate showed a tendency to vary inversely with the age. All the cases under one year of age had a pulse rate of between 72 and 60 per minute; the four between one and three years had rates varying between 66 and 37; in those between six and fifteen years the rate varied between 48 and 37 except in one case where a child of eight years had a pulse rate of 20 per minute. In the two adults, aged 22 and 23 years, the pulse rates were 43 and 34 respectively.

Cyanosis, dyspnœa and syncopal attacks are not prominent features of the condition, and their occurrence is probably dependent on the extent of the cardiac deformity rather than on the degree of block.

The two cases described in this paper fall into line with those previously recorded. They both presented physical signs compatible with defect in the inter-ventricular septum, and in Case 2 other lesions probably of congenital origin (e.g., pulmonary stenosis) were present. In the first case there was no disability except for the history of syncope three weeks before admission. In the second, however, cyanosis, clubbing of the fingers, dyspnœa on exertion and syncopal attacks are recorded. All these might well be accounted for by the magnitude of the cardiac deformity. In Case 1 neither atropine, adrenalin nor exertion influenced the block in the slightest degree, and in Case 2 it is clear that neither exertion nor atropine abolished the block.

From a study of the literature it seems probable that congenital heart block is confined to cases where there is a defect in the inter-ventricular septum

and that in the absence of gross cardiac deformities the block per se causes little or no disability. It is, however, not always easy to say definitely that the block is of congenital origin. A considerable number of cases of heart block in children following the acute infections have been described, but where a history suggesting such a cause is lacking, and where there are definite physical signs of congenital deformity, the probability is strongly in favour of a congenital origin for the block.

In view of the fact that practically all the cases presented physical signs suggestive of patent inter-ventricular septum, and that of all deformities this is the one most likely to interfere with the normal course of the a-v bundle, it seems probable that the presence of heart block in congenital heart disease is an important positive sign of defect of the posterior part of the interventricular septum.

SUMMARY.

Two cases of heart block in congenital deformity of the heart are described.

In one the block was complete and in the other it was partial. In neither case was the block of nervous origin. Cyanosis and dyspnœa were present in one case but not in the other.

The probable lesions were patent inter-ventricular septum and maldevelopment of the a-v bundle, though in both cases there may have been other cardiac deformities.

REFERENCES.

1. Wilson, J. G., and Grant, R. T., *Heart*, Lond., 1926, XII, 295.
2. Abbott, M., Osler W., and McCrae, T., *Modern Medicine*, London, 1927, IV, 687.
3. White, P. D., Eustis, R. S., and Kerr, W. J., *Am. J. Dis. Child.*, Chic., 1921, XXII, 299.
4. Rhomberg, E. C. and White, P. D., *Bost. Med. and Surg. J.*, Boston, 1924, CXC, 591.
5. Frias, J. B., quoted by Abbott, *loc. cit.*, 667.
6. Barbier, Lebée and Mouquin, *Arch. d. Mal. de Coeur*, Paris, 1922, XV, 171.
7. Lukin, N. and Frey, D., *Arch. of Ped.*, N.Y., 1927, XLIV, 646.
8. McIntosh, R., *Am. J. Dis. Child.*, Chic., 1927, XXXIV, 965.
9. Nissé, B. S., *Proc. Roy. Soc. Med.*, London, 1928, XXI (Clin. Sec.), 438.
10. Schlesinger, B., *Proc. Roy. Soc. Med.*, London, 1927, XXI (Sec. Dis. of Child), 215.